An Evaluation of Stressor Interactions in the Great Lakes

A report submitted to the
International Joint Commission by the
Science Advisory Board
Science Priority Committee
Interacting Stressors Work Group

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List of Acronyms

IJC	International Joint Commission
MARS	Managing Aquatic ecosystems and water Resources under multiple Stress
PBT	persistent, bioaccumulative and toxic pollutants
PCBs	polychlorinated biphenyls
PFAS	per- and polyfluoroalkyl substances
POP	persistent organic pollutants
VHS	viral hemorrhagic septicemia

Executive Summary

An environmental stressor is any factor whose presence adversely affects individuals, populations, or ecosystems. Often but not necessarily the result of human activities, examples include many different pollutants, excess nutrients, habitat loss and invasive species. Recognizing that interactions among multiple stressors in the Great Lakes are poorly understood, the International Joint Commission's (IJC) Science Advisory Board undertook a review and exploratory analysis. The project included a facilitated expert workshop and a review and assessment of the literature from within and beyond the Great Lakes basin. This was followed by focused consideration of 11 stressor pairs selected as important for the Great Lakes. Assessment of stressor interactions is necessary to understand cumulative stress from multiple stressors. It is possible for a single stressor to dominate, for combined effects to equal or exceed the effects of two stressors acting alone or for one stressor to partly or strongly counteract another.

The ecological literature is increasingly attentive to the potential importance of multiple interacting stressors. Review of this literature finds reasonable consensus on definitions of categories of stressor interactions. Considering two possible stressors that may or may not interact with one another, an **additive** outcome is when the combined influence is equal to the sum of individual effects. The term **synergy**, often used for any type of stressor interaction, is defined as a combined influence greater than the sum of individual effects. **Antagonism** occurs when one stressor mitigates the effects of a second.

Recent literature reviews and formal syntheses find support for additive, synergistic, and antagonistic outcomes across a variety of stressor combinations. Synergistic and antagonistic effects both were common in published studies, with additive effects less so, based on four syntheses of aquatic ecosystem studies, including one specifically focused on studies pertaining to the Great Lakes. However, recent work from Europe—dominated by studies of river systems and smaller lakes—reported that additive effects were most frequent. At this time, it is difficult to know whether these differing outcomes should be attributed to differences in terminology and methods, differences in geography and habitat type, or the particular stressor combinations and ecosystem responses for which sufficient information is available. Regardless of the form of interaction, the studies agree that two or more stressors can interact to produce stress on the ecosystem that is greater than one acting alone, resulting in greater overall cumulative stress.

Based on existing literature and professional judgment, this report examines seven priority stressors to capture the breadth of stressors within the Great Lakes:

- invasive species,
- toxic chemicals,
- nutrients,
- climate change,
- habitat loss,
- fish harvest, and
- pathogens.

Further analysis was restricted to interactions between pairs of stressors, while acknowledging that interactions between multiple stressors may occur. Of the 21 possible pairwise interactions, eleven were selected for consideration based on existing literature, work group and workshop discussions, and professional judgment. Each stressor pair was first considered at a high level (e.g., toxic chemicals and nutrients), and then with a more specific example (e.g., organic pollutants and phosphorus) to determine whether existing knowledge could indicate if the two stressors were likely to be mutually enhancing (resulting in an additive or synergistic result), whether one might counteract the other (antagonism), or both.

The 11 stressor pairs examined in detail as part of this report found the following generalized relationships:

Usually antagonistic

- organic pollutants and phosphorus

Usually additive or synergistic

- Dreissenid mussels and phosphorus
- wetland loss and *Phragmites*
- multiple invasive species and fish harvest
- multiple invasive species and climate warming
- climate change and wetland loss
- precipitation and phosphorus
- phosphorus and wetland loss

Both additive/synergistic and antagonistic

- mercury and wetland loss
- organic pollutants and climate change
- precipitation and pathogens

Key Findings and Recommendations

Stressor interactions in the Great Lakes are important to consider and are likely to result in an overall increase in cumulative ecosystem stress. However, at this point in our understanding of stressor interactions in the Great Lakes, there is no clear resolution to the question of whether to continue traditional stressor-by-stressor management, or to adopt more holistic, integrated management of stressors within an explicit framework of interacting stressors. There is a need for continued attention to this issue, using the infrastructure, organizations and governance systems that already exist in the Great Lakes basin.

Ecosystem responses to both individual stressors and interacting stressors may be nonlinear whereby ecosystems can be pushed beyond tipping points that often cannot be anticipated, raising the possibility of rapid system decline that may be difficult to reverse. This presents an argument for intensified investment in monitoring and research on stressor interactions. The IJC Science Advisory Board – Science Priority Committee finds that robust studies of interactions are rare, and often limited to controlled laboratory settings or mesocosms and single species or life stages.

> **Recommendation 1: That the Parties[1] and other stakeholders that support Great Lakes monitoring and research programs investigate the gaps in understanding of stressor interactions described in this report, with an emphasis on those stressor interactions that are both most likely to impact natural environments across a range of environmental conditions and be amenable to management intervention at appropriate scales.**

This report's analysis highlights the importance of understanding which stressor interactions are additive, synergistic or antagonistic, as they have different consequences for cumulative stress. There are existing Great Lakes management programs that consider stressor interactions (e.g., Areas of Concern, Great Lakes fishery management) and those programs may hold promise for improved understanding of the management of stressor interactions, and for development of management approaches that explicitly consider interactions.

Adaptive management is an important framework for managing interacting stressors. Application of this framework will benefit from ongoing assessment of how understanding of stressor interactions has changed due to additional research and practical knowledge gained from management actions that have produced unexpected results, either positive or negative.

> **Recommendation 2: That any management actions in the Great Lakes by the Parties, state and provincial governments, and Tribes, First Nations and Métis governments should be targeted toward interactions that are best understood. Current management approaches that consider multiple stressors should be incorporated into**

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[1] The Great Lakes Water Quality Agreement defines the Parties as the Government of Canada and the Government of the United States.

approaches for addressing the interactions of other combinations of multiple stressors.

Spatial and temporal variability in the occurrence of individual stressors and long-term trends in their intensity are important contextual considerations in the evaluation of stressor interactions. Because the majority of stressors originate on land where agricultural and urban activities are most pronounced, the intensity of many stressors is likely to be greatest in nearshore waters and decrease with distance from shore. In addition, stressor frequency and duration, as well as the sensitivity and vulnerability or resilience of the impacted resource, can vary with weather extremes, ecosystem conditions and drivers of human activity. In some cases, the analysis of interactions may be required at a relatively fine spatial and temporal scale.

Recommendation 3: Lessons learned from science and management efforts that identify important stressor interactions should include spatial, temporal and other contextual information that can provide critical information on transferability of information.

Climate change is the most pervasive stressor that merits further consideration in terms of its interaction with other stressors, including those described in this report (toxic chemicals, invasive species, habitat loss, nutrients and pathogens). Given the global nature of climate change drivers, regional management of climate change may have limited potential to ameliorate impacts in the region, despite the incremental value that actions to reduce regional contributions to global climate change may have. This highlights the importance of climate adaptation and managing for resilience.

Recommendation 4: That the Parties tailor their Great Lakes science and management programs to explicitly consider how the multiple facets of climate change may interact with other stressors, and manage wherever possible toward enhancing resilience.

1.0 Introduction

There is growing appreciation that management of large, complex ecosystems must deal with multiple human stressors rather than focusing on a single stressor at a time. There is also ample evidence of significant, adverse changes to the Great Lakes attributable to multiple stressors, including the anoxic/hypoxic zone of central Lake Erie, the rapid disappearance of the widespread benthic amphipod *Diporeia*, the invasion of Dreissenid zebra and quagga mussels, wetland loss, declines in native fish populations, and nuisance algal blooms in western Lake Erie, Green Bay, and elsewhere. Cumulative stress from multiple stressors is difficult to assess due to the challenge of quantifying their individual effects and limited knowledge of their interactions. However, recent studies highlight the relevance of cumulative impacts of multiple stressors and the potential for significant and adverse impacts on the lakes (e.g., Allan et al. 2013; Danz et al. 2007; Morrice et al. 2008; Smith et al. 2015). A group of researchers seeking to identify a research agenda for the Great Lakes included the need to better understand stressor interactions in one of its five grand challenges:

> it is clearly necessary to adopt a more comprehensive approach to understanding human-induced degradation rather than a case-by-case approach examining single stressors. Furthermore, there is an urgent need to understand whether the ecosystem response to multiple stressors is simply additive, or involves synergistic or antagonistic effects and to understand the resilience and resistance of the Laurentian Great Lakes to both stressors and climate variability (Sterner et al. 2017).

The Science Advisory Board of the International Joint Commission (IJC) convened a Stressor Interactions Work Group to complete this study because it recognized the lack of understanding of the potential for nonlinear effects and unanticipated, possibly sudden, ecological changes that may result from the additive and nonadditive interactions of several stressors. The group recognized that the degree and direction of interaction among Great Lakes stressors is difficult to predict, and that the net impacts of two or more stressors on the same ecosystem are not routinely considered in ecosystem management and restoration decisions. The goal of the project was to characterize stressor interactions in the Laurentian Great Lakes, with emphasis on a set of priority pairs of stressors. This report includes a high-level summary of multistressor literature both within and outside the Great Lakes, an overview of seven priority stressors in the lakes, and consideration of 11 stressor pairs whose interactions believed to be the best documented and most important. The report concludes that (1) much evidence points to the co-occurrence of multiple stressors, (2) stressor interactions indeed occur, and (3) cumulative stress is real but difficult to determine, and should not be thought of as a simple summation of individual impacts. Given existing uncertainties, further research into the interactions of multiple stressors in natural environments will benefit management decisions.

2.0 Approach

The project approach centered around four tasks described in the original statement of work. A contractor (LimnoTech) led each task, with additional input and review by a work group (see acknowledgements). The first task was to: review existing literature that considers stressor interactions, including marine and other literature from outside the Great Lakes; develop a working vocabulary of stressor interaction terms; summarize the state of knowledge, and; generate an annotated list of key references. The second task was to develop a list of priority stressors affecting the Great Lakes, and then identify approximately ten stressor pairs where interactions potentially are important and can be evaluated. The third task was to convene an expert workshop with work group members and others, including participants from academic, government and non-government sectors, to evaluate progress under the first and second tasks, and further explore the nature of interactions among stressors. The fourth task was to prepare a project report[1] that addresses the state of knowledge of stressor interactions in the Great Lakes, identifies and describes up to 10 pairs of ‘priority’ interacting stressors, including their spatial variability and severity across the lakes, identifies key knowledge gaps, and recommends science and policy priorities to address or further evaluate the importance of stressor interactions in the Great Lakes.

3.0 Findings – Literature Review

3.1 Conceptual frameworks for stressor interactions

In a widely cited early investigation of interactions among multiple stressors, Folt et al. (1999) suggested three theoretical models: comparative, additive, and multiplicative. These refer, respectively, to cases where the effect is simply that of the single worst stressor (e.g., a limiting factor), the effects are purely additive or another stressor further modifies the effect of one stressor. Comparative refers to the case where one stressor trumps all others. Multiplicative refers to any case where the interaction between stressors is not strictly additive (e.g., it includes both synergistic and antagonistic). Over the years, the uses of these terms by others have not always been consistent. In a review of some four decades of discussion of synergies in the ecological literature, Côté et al. (2016) highlight inconsistencies in the use of terms synergistic, antagonistic and additive, among others. Further, despite frequent reference to synergistic interactions, their review finds antagonisms to be more common. **Table 1** (next page) further defines terms.

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[1] The full contractor project report is available at: ijc.org/sites/default/files/2020-03/SAB-SPC_StressorInteractions_ContractorReport_2020.pdf.

Table 1: Definitions of terms related to stressor interactions used in this report

Definition of Terms	
Additive	Combined stressor impacts that are equal to the sum of the individual impacts
Antagonism	Combined stressor impacts that are less than the sum of the individual impacts
Cumulative	The influence of all stressors together, often estimated as an additive summation
Multiplicative	Stressor impacts are synergistic or antagonistic rather than additive
Synergy	Combined stressor impacts that are greater than the sum of the individual impacts

Smith et al. (2019) presented a conceptualization of three possible outcomes for the interaction of two individual stressors, A and B (**Figure 1**, next page). For the purposes of this report, an additive effect occurs when the combined influence of two stressors is equal to the sum of the two individual stressors when acting alone, with no net interaction. A synergistic effect is recognized when the influence of two stressors together is greater than the sum of their individual effects. An antagonistic effect includes any example where the influence of two stressors acting together is less than the sum of their independent effects. Another reference point is seen when the combined influence of two stressors is no greater than the influence of the more severe stressor acting alone. Sometimes referred to as "comparative," this corresponds to the "Law of the Minimum" concept, which posits, for example, that whatever nutrient is in least supply determines productivity. It should be noted that additive, synergistic, and antagonistic all refer to situations where the combined effect of two stressors is greater than either acting alone. It is also possible for a second stressor to reduce the influence of a primary stressor, referred to as a mitigative effect or reversal, although this is less commonly reported. These definitions are also consistent with others who have presented a conceptual representation of multiple stressors effects (Birk and Hering, 2018; Gunderson et al. 2016; Smith et al. 2019).

3.2 Evidence of stressor interactions

Recent literature reviews and formal syntheses find support for additive, synergistic, and antagonistic effects of stressor combinations. A synthesis of 171 studies that manipulated two or more stressors in marine and coastal systems found that synergistic and antagonistic interactions were about equally common (36 percent and 38 percent, respectively) and additive effects less common (26 percent) (Crain et al. 2008). A meta-analysis that analyzed data from 88 papers including 286 responses of freshwater ecosystems to paired stressors reported that the net effects of stressor pairs were more frequently antagonistic (41 percent) than synergistic (28 percent) or additive (16 percent) (Jackson et al. 2016). That study also reported that in 15 percent of the cases, the combined influence of two stressors was less than either stressor alone. However, in most cases reported as antagonisms, the combined influence of two stressors is still greater than either stressor alone, as shown in **Figure 1**.

In a recently published literature review of Great Lakes stressor interactions, Smith et al. (2019) found that synergies accounted for 49 percent of the total interactions, antagonisms for 42 percent, and relatively few studies (9 percent) reported additive effects. While fewer additive effects were reported from that study than by Crain et al. (2008) and Jackson et al. (2016), these Great Lakes-specific results nonetheless point out the challenge of predicting the cumulative effects of stressors when both synergies and antagonisms are widespread. Finally, a meta-analysis of 112 studies of multiple stressors in freshwater, marine and terrestrial communities found additive effects in less than one-fourth of the cases reviewed, and antagonisms were more common than synergies (Darling and Côté, 2008).

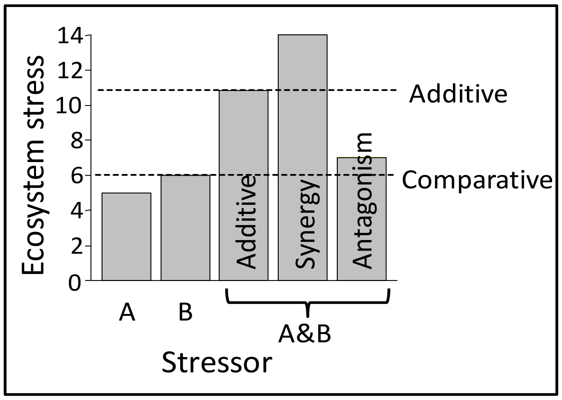


Figure 1: Conceptualization of interactions among stressors (from Smith et al. 2019).

Comparing these four studies (**Figure 2**), antagonisms were consistently near 40 percent, synergistic outcomes ranged from 28 to 49 percent and additive effects ranged from 9 to 26 percent. Although some differences are seen among these studies, it is noteworthy that nonadditive effects are considerably more frequent than strictly additive. Interestingly, these studies do not report cases where a single stressor has such

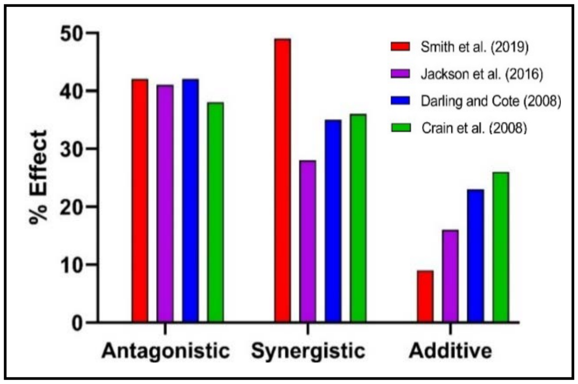
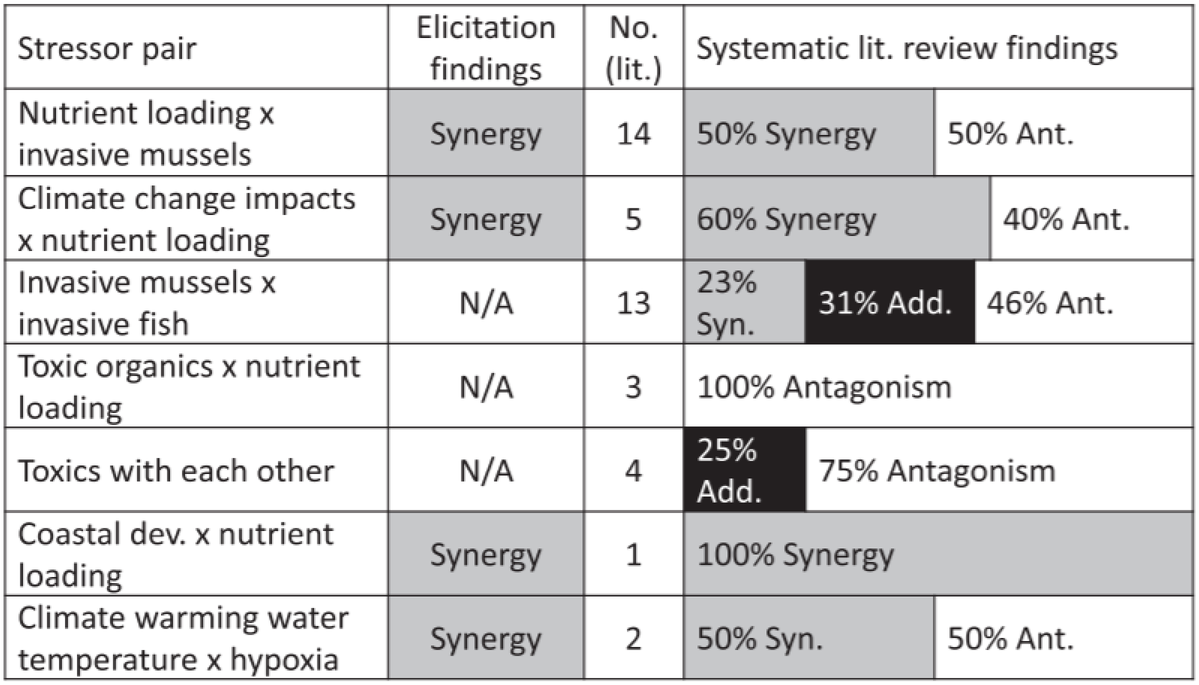


Figure 2: Results from four peer-reviewed literature compilations that identify the number of studies that found antagonistic, synergistic and additive effects.

strong negative effects that the effects of a second stressor are not detected. This may reflect a kind of publication bias, where meta-analyses of interacting stressors focus on studies where multiple stressor effects are at least suspected to occur.

In the only study of stressor interactions focused on the Great Lakes, Smith et al. (2019) performed an extensive systematic literature review along with expert elicitation to identify priority pairs of likely or potentially important interactions in the Great Lakes. **Figure 3** shows the results of the literature findings, where the most studied pair was nutrient loading and invasive species, followed by invasive mussels and invasive fish. Expert elicitation frequently identified synergy as the probable form of interaction, and often was inconsistent with the systematic literature review. The review showed that while there are many potential interactions in the Great Lakes, studies among co-occurring stressors were limited and few measurements of both individual and joint effects of stressors had been published. This was also noted in a summary of the challenges for research in the Great Lakes by Sterner et al. (2017), where they articulated the importance of focusing attention on developing a more comprehensive approach to understanding human-induced stress than simply examining single stressors on a case-by-case basis. Furthermore, Sterner et al. (2017) stressed that, while understanding interactions is important, we also need to understand the resiliency of the Great Lakes to multiple stressors. Indeed, while the concept of resiliency is not discussed in depth here, it remains an important consideration in understanding how the Great Lakes ecosystems will respond to additional stress. Knowing the potential capacity for the ecosystem to absorb and recover from change may help to better predict what changes (both structurally and functionally) within an ecosystem is expected.



Stressor pair	Elicitation findings	No. (lit.)	Systematic lit. review findings		
Nutrient loading x invasive mussels	Synergy	14	50% Synergy	50% Ant.	
Climate change impacts x nutrient loading	Synergy	5	60% Synergy	40% Ant.	
Invasive mussels x invasive fish	N/A	13	23% Syn.	31% Add.	46% Ant.
Toxic organics x nutrient loading	N/A	3	100% Antagonism		
Toxics with each other	N/A	4	25% Add.	75% Antagonism	
Coastal dev. x nutrient loading	Synergy	1	100% Synergy		
Climate warming water temperature x hypoxia	Synergy	2	50% Syn.	50% Ant.	

Figure 3: Systematic literature review of potential interactions in the Great Lakes (from Smith et al. 2019).

In contrast to the findings reviewed above, a recent effort in the European Union to evaluate multistressor effects concluded that the majority were additive. The Managing Aquatic ecosystems and water Resources under multiple Stress (MARS) Project[1] (Hering et al. 2015) found that:

> Out of 156 single results of pair-wise stressor combinations analyzed within studies of MARS, two-thirds were additive (i.e. had no significant interactions), while one third showed significant interactions (Birk and Hering, 2018).

It should be noted that MARS considered significant interactions to be non-additive (e.g., synergistic or antagonistic) when the effect of the two stressors was greater than or less than their sum. The MARS results suggest that in European aquatic systems,[2] stressor interactions beyond simple additivity are less common. Some aspects of the MARS study may be relevant to considerations of its applicability to the Great Lakes, including the range of aquatic ecosystem types examined, and an emphasis on nutrients and physical variables (temperature and hydrology). Regardless, this project clearly adds evidence that multi-stressor influences warrants consideration.

At this time it is difficult to know whether the range of outcomes from these efforts to generalize about multistressor effects should be attributed to differences in terminology and methods, or to the particular stressor combinations and ecosystem responses for which sufficient information is available. Should broad general principles regarding stressor interactions emerge from studies in similar ecosystems around the world, or are watersheds, species assemblages or ecoregions idiosyncratic? Should marine and freshwater systems be expected to behave similarly? Should the same pair of stressors be expected to interact in a similar fashion in different ecosystem settings? Côté et al. (2016) emphasize the need to consider uncertainty in making management decisions.

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[1] For more on the MARS project, visit mars-project.edu.

[2] Mostly rivers (42 percent of 130 total water bodies studied) and some lakes (24 percent) and coastal waters (34 percent) impacted by nonpoint pollution and hydrologic alteration.

4.0 Main Insights from Workshop

The work group convened a two-day workshop as part of this project, attended by 23 subject matter experts, plus IJC staff and contractors (see **Appendix** for April 9 and 10, 2019 workshop attendance). The purpose of the workshop was to confirm stressor pairs thought to be most important in the Great Lakes, characterize their interacting effects and variability across the Great Lakes, and assess the underlying mechanistic understandings associated with priority stressor pairs. Workshop discussions benefited from background material prepared in advance by the contractors.

Five speakers, asked to comment on specific stressors, raised important concepts to guide further discussion. It was noted that interactions among different chemicals have received extensive consideration, particularly in regard to human health. A historical review of invasive species impacts on Great Lakes fishes and fisheries provided an example where one or a few invasive species acting in different time periods were of overriding importance, suggesting that additional stressors likely were of minor importance. It was noted that while many stressors are likely congruent, spatial overlap of stressors should not be assumed, and spatial context (nearshore vs. offshore, individual lakes, embayments) is an important consideration. It also was noted that habitat loss is a complicated stressor to consider, as habitat loss can be both a stressor and a response. With regard to climate, a key consideration is whether the stationarity assumption that underlies hydrologic and other climate predictions remains operable, as a changing climate introduces considerable uncertainty into predictions about future conditions.

Discussions over the two-day workshop emphasized a number of complexities in assessing the potential for stressor interactions. Participants agreed that an analysis and characterization of stressor pairs is highly location specific. Context, which includes location, yet goes well beyond it to include the many environmental variables that differ among locations, is an important aspect of stressor pair impacts. This can also include, among other considerations, a social dimension (e.g., the perceptions of a ‘user’ of the Great Lakes system). As the IJC is most interested in management-relevant recommendations, as opposed to those that are limited to a call for more research, this aspect was considered during review of potential stressors for analysis. Participants recognized climate change as an ‘overlying’ stressor that affects most, if not all others. Management recommendations were considered to be best suited for stressor pairs where data, information and understanding of interactions are sufficient to offer recommendations with confidence.

There was general agreement that the term ‘stressor,’ as illustrated by the proposed stressor categories, may be too broad. Considering more specific stressors (specific species, chemicals, aspects of a changing climate, *et cetera*) may be more helpful, and the evaluation may need to be more outcomes driven. The proposed stressors were also considered to be uneven and it was recommended that they be redefined to be more uniform in their breadth (e.g., either all broad or all narrow). Human activity was mentioned as a significant driver of all of the stressors, but the driver activities were not specifically identified.

A key goal of the workshop was to confirm a list of priority interacting stressors and their associated information (e.g., spatial extent, severity), building from an initial draft matrix that was prepared in advance. Stressor pairs were selected based on the criteria that:

1. at least one of the stressors is thought to be important and potentially modified by the presence of a second stressor, and

2. information exists to assess interactions directly, or sufficient understanding exists to develop conceptual models and hypotheses that identify mechanistic pathways to clarify how pairs of stressors may interact.

This led to the final list of seven priority stressors: invasive species, toxic chemicals, nutrients, climate change, habitat loss, fish harvest, and pathogens. The discussion of interacting stressors in the following section incorporates the results of these workshop discussions.

5.0 The Potential for Stressor Interactions in the Great Lakes

5.1 Priority stressors

Based on work group discussion and contractor literature review, seven priority stressors were selected to capture the breadth of stressors within the Great Lakes. Brief descriptions of the selected stressors are below. It is acknowledged that such a list inevitably is incomplete, but it was important to restrict the list in order to assist in the subsequent step of identifying a list of priority stressor pairs.

Invasive species: Invasive species are among the greatest threats to the Great Lakes basin. Researchers have identified the Great Lakes as one of the most invaded freshwater systems across the world (Ricciardi and MacIsaac, 2000; Ricciardi 2006). At present, more than 180 species are identified as nonindigenous to the region (Sturtevant et al. 2019). Most nonindigenous species do not cause harm to the environment, the economy or human health. Those that do cause harm are considered invasive, such as sea lampreys, dreissenid mussels, round gobies and the wetland plant *Phragmites.* Given their expansive distributions across both nearshore and offshore Great Lakes environments, these invasive species are likely to interact with most other types of stressors as well as other invasive species. However, the extent and severity of these interactions can vary across time and space.

Toxic chemicals: A number of anthropogenic chemicals can be found within the Great Lakes basin including persistent organic pollutants (POPs) as exemplified by dichloro-diphenyl-trichloroethane, or DDT; polychlorinated biphenyls (PCBs); polychlorinated dibenzo-p-dioxins (dioxins) and dibenzofurans; per- and polyfluoroalkyl substances (PFAS); and many other emerging chemicals (e.g., pharmaceuticals, personal care products). This report focuses primarily on chemicals with a long history and widespread occurrence within the Great Lakes: POPs (mainly PCBs), and the metal, mercury. PCBs have undergone a significant decrease across all lakes since their ban in the 1970s, and mercury concentrations in fish tissue have also shown a gradual decline, followed by a gradual stabilization (Visha et al. 2018). However, most restrictive fish consumption advisories are still driven primarily by PCBs and secondarily by mercury (Gandhi et al. 2017a, 2017b; Ontario Ministry of the Environment and Climate Change 2015). While the discussion here will focus on the interaction of single toxic compounds or classes with stressors other than different toxic chemicals, the potential for within-category interaction should not be forgotten. For example, there is growing interest in the influence of chemical mixtures in relation to fish consumption advisories (e.g., Gandhi et al., 2017b). Individual contaminants in the presence of many other contaminants can induce a variety of interactions including additive and synergistic effects.

Excess nutrients: Nutrients, such as phosphorus, nitrogen and silica, are essential components of phytoplankton growth and hence of the base of the Great Lakes food web. However, excess loads of nutrients (mainly phosphorus) from point and nonpoint sources can lead to excessive algal growth, including harmful algal blooms that cause ecological and human health concerns. Phosphorus has been recognized for decades as the main limiting nutrient for primary productivity in most freshwater systems, including the Great Lakes. High levels of phosphorus result in severe eutrophication symptoms, including algal blooms and oxygen depletion of bottom waters, leading to regulatory efforts by the United States and Canada beginning in the 1970s, and accelerating through the 1990s and early 2000s (Dove and Chapra, 2015). The reappearance of large algal blooms and continuing hypoxia in parts of Lake Erie and other parts of the Great Lakes in the mid-2000s have been attributed to a rise in loading of dissolved phosphorus, much of which originates from agricultural tile drains (Smith et al. 2015), and higher runoff in recent years (Stow et al. 2015) attributed by some to changing climate. Excess nutrients are known to interact with other stressors, notably dreissenid mussels and climate. In addition, co-limitation of algal growth by nitrogen and phosphorus is an area of growing concern.

Habitat loss: Decline of coastal wetlands is a principal habitat concern in the Great Lakes, as well as direct alterations of habitat including dredging and filling, hardening of shorelines, and construction of dams and other barriers that restrict fish passage in tributaries and modify flows. A significant portion of the biological productivity and diversity within the Great Lakes is concentrated in the coastal wetlands. However, land clearing and drainage for agriculture and filling of wetlands to permit coastal development have resulted in the loss of significant portions of Great Lakes wetlands (Shuchman et al. 2017). Some experts have estimated that nearly 50 percent of the pre-settlement Great Lakes coastal wetlands have been lost; in some areas such as Saginaw Bay in Lake Huron, up to 95 percent have been lost. Additionally, invasive plants such as *Phragmites* and *Typha* have replaced a significant portion of native wetland plants. These factors continue to threaten the quality of existing wetlands (Trebitz et al. 2009). The loss of wetlands can interact directly with other Great Lakes stressors, including climate change, nutrients and toxic chemicals. For example, wetlands can sequester toxic chemicals and trap nutrients from entering the main waterbody such that the loss of wetlands leads to additional contaminant loads in the main water bodies.

Climate change: Climate change has significant impacts on the Great Lakes basin, affecting multiple aspects of the aquatic ecosystem, including air temperature, precipitation intensity and timing, length of growing season, and lake ecology and indigenous wildlife distributions, as well as human activities (Environmental Law and Policy Center 2019). Evidence of this change is seen in multi-decadal trends in ice cover and surface water temperature across the Great Lakes since the 1970s (Mason et al. 2016). According to the Environmental Law and Policy Center 2016 report,

> Between 1901-1960 and 1985- 2016, the Great Lakes basin has warmed 1.6°F in annual mean air temperature, exceeding average changes of 1.2°F for the rest of the contiguous United States. By the end of the 21st century, global average temperatures are expected to rise an additional 2.7°F to 7.2°F.

While a changing climate has a wide range of effects, for this project the primary stressors considered were warming and precipitation. The Great Lakes region saw an almost 10 percent increase in precipitation from 1901 to 2015 (the United States increased just 4 percent), with more of this precipitation coming as unusually large events (Environmental Law and Policy Center 2019). Similarly, on the Canadian side of the basin, damage from localized heavy rainfall is increasing (Environmental Commissioner of Ontario 2018). Climate change is likely to interact with other stressors, although the interaction type and strength can vary both seasonally and temporally. For example, increased temperatures can both provide new refuge for some invaders yet reduce the densities of cooler water invaders in the southern Great Lakes. Warmer water temperatures can enhance the mobility of toxic chemicals but may also increase microbial breakdown of some contaminant groups. Likewise, warmer temperatures may intensify algal blooms but reduced spring snow melt may also reduce runoff.

Pathogens: Important pathogen concerns in the Great Lakes include those leading to beach advisories and closings often based on fecal indicator bacteria, as well as fish disease such as viral hemorrhagic septicemia (VHS). Disease transmission through the contamination of recreational and drinking water sources is a significant public health concern in the Great Lakes (Corsi et al. 2015; Lenaker et al. 2017). While fecal indicator bacteria (e.g. *E. coli*) are the prominent measure of contamination, recent research has demonstrated that fecal indicator bacteria can sometimes be poor surrogates for certain pathogens (Corsi et al. 2015; Ishii et al. 2014), and viruses are also likely responsible for a portion of illness resulting from recreational water exposure. Indeed, there are over 500 waterborne pathogens of potential concern in drinking waters, identified by the US Environmental Protection Agency (Ashbolt 2015), and both countries have developed treatment goals or drinking-water parameters based on pathogen and microbial risk assessment (Ontario Safe Drinking Water Act, US Safe Drinking Water Act). Pathogenic organisms can closely interact with other stressors, including toxic chemicals, warming, habitat loss and fishery overharvest. For example, VHS, an invasive virus caused by an aquatic rhabdovirus, has affected many different fish species from different families in the Great Lakes and is responsible for significant fish mortality (Elsayed et al. 2006). The largest outbreak in the Great Lakes region to date was in 2006, with fewer reported outbreaks across the region since 2011 (Stepien et al. 2015). This suggests the population may be developing some level of immunity to the virus (Millard and Faisal, 2012), although it still remains a concern (Getchell et al. 2019). Pathogenic organisms also interact with climate change, where increases in precipitation can lead to higher bacteria and virus loads in nearshore Great Lakes environments. Pathogens are a concern for human health as well as ecosystem condition.

Fish harvest: Improperly managed fishery exploitation can be an important threat to sustainable fish populations and healthy ecosystems in the Great Lakes and elsewhere. Historically, overharvesting has caused significant reduction or near extirpation of several commercial species of the Great Lakes, including cisco, lake whitefish, and walleye (Brenden et al. 2010; Ebener et al. 2008; Hansen et al. 2019; Haponski and Stepien, 2016), and near-extirpation of the lake sturgeon (Sweka et al. 2018). In addition, fisheries declines have been exacerbated by contaminants such as dioxin, known to result in poor lake trout reproduction historically (Cook et al. 2003). The Great Lakes Fishery Commission now facilitates binational stock assessments and harvest decisions to ensure a well-balanced and productive fish population that supports recreational, commercial or subsistence fisheries, as well as healthy ecosystems. This cooperative fishery management has been critical as management of stocks requires an understanding of other stressors such as invasive species, habitat loss and climate change that will impact sustainable harvest quantities (de Kerckhove et al. 2015). For example, while lake trout were also subjected to overfishing, the invasive sea lamprey has caused the most damage to this species (Elrod et al. 1995), and warming from climate change is expected to have a significant effect on the distribution and abundance of Great Lakes fish (Collingsworth et al. 2017; Lynch et al. 2010; Minns 2014). Understanding how these stressors interact remains an important component of regional fisheries management strategies.

5.2 Important pairwise stressor interactions

Of the 21 possible pairwise interactions among seven priority stressors, eleven were selected for consideration based on existing literature, work group and workshop discussions, and professional judgment (**Table 2**, next page). As with identification of priority stressors, it is acknowledged that any list of important pairwise interactions may omit others worthy of consideration. For each potential pairwise interaction, this report attempts to assess whether an interaction is plausible based on what is known about the mechanistic pathways linking the two individual stressors. In each case, specific examples are drawn upon to explore the range of potential interactions within the higher-level category. Three of the pairs were also selected as workshop case studies, providing opportunities to incorporate diverse perspectives and to explore any additional factors that may influence the likelihood and expression of an interaction.

It should be emphasized that the following explorations of pairwise stressor interactions is based on an interpretation of likely pathways and existing evidence. This was considered sufficient to provide reasonable assessment of the likelihood that an interaction is additive or synergistic, meaning that the combined impact of the two stressors together was likely as great as or greater than their sum; or antagonistic, meaning that at least one of the two stressors had some likelihood of reducing the influence of the other. While speculative to some degree, evidence from the literature generally supported these interpretations. At a minimum, this exercise helps to determine first whether an interaction is plausible enough to warrant further attention, and second, whether the presence of the second stressor is likely to enhance the impact of the first (enhance system overall stress), or offset its influence.

Table 2: The eleven stressor pairs identified from seven priority stressors, selected for their potential to interact in ways that may enhance or offset the harmful influence of one or both acting alone. Explanation of the interaction, most probable interaction type and location where the interaction may be of greatest concern all focus on the specific example given. See text for further explanation.

Stressor Pair	Specific Example	Type of Interaction (additive/synergistic vs antagonistic)	Areas most affected
Toxic chemicals and nutrients	Organic pollutants and phosphorus*	Antagonistic (most probable): higher fish biomass due to nutrient enrichment and increased productivity results in biomass dilution of toxins and greater organic matter burial. Additive/synergistic: Nutrient induced hypoxia could enhance mobility and microbial transformation of some toxic chemicals (e.g., methylation of Hg), and possibly bioavailability.	Areas of Concern and areas impacted by agricultural and urban runoff, and wastewater
Invasives and nutrients	Dreissenid mussels and phosphorus*	Additive or synergistic (most probable): Nearshore shunt traps nutrients nearshore, reducing offshore productivity; increased water clarity due to mussels promotes benthic algal growth; selective feeding of mussels on diatoms vs. cyanobacteria promotes HABs. Antagonistic: mussel feeding may sequester nutrients in sediment; *Phragmites* may trap nutrients in coastal areas.	Near ports in embayments and nearshore areas of lower lakes
Habitat loss and invasives	Wetland loss and *Phragmites**	Additive or synergistic (most probable): Invasive plants outcompete native plants in wetlands, and degradation of wetland habitat due to development and water level changes can enhance invasive colonization. Shoreline hardening also can create habitat favorable for round gobies.	Near developed land and natural coastal wetland areas, especially in more southerly sites
Toxic chemicals and habitat loss	Mercury and wetland loss	Additive or synergistic: Wetland plants and sediments immobilize nutrients and contaminants, serving as sinks, such that wetland loss can exacerbate contaminant or nutrient loads. Antagonistic: Wetlands are important sites for conversion of mercury into potentially more toxic and bioaccumulative methylmercury.	Areas of Concern and wetlands around shallow bays and connecting channels
Toxic chemicals and climate change	Organic pollutants and warming	Additive or synergistic: Warmer temperatures enhance mobility and microbial transformation of some toxic chemicals (e.g., methylation of mercury), and possibly bioavailability. Antagonistic: Warming may accelerate microbial degradation rates and annual duration of activity impacting some organic pollutants.	Urban areas, ports, connecting channels, and tributaries
Invasives and fish harvest	Multiple invasives and fish harvest	Additive or synergistic (most probable): Sea lamprey can reduce native fish populations thereby impacting fish harvest regulations, mussels can affect pelagic food web, reducing energy available to higher trophic levels. Antagonistic: Improved water clarity due to mussels enhances feeding conditions for Lake Ontario salmon.	Offshore areas of deeper lakes or basins (impacts on fish food supply)
Invasives and climate change	Dreissenid mussels (and other invasives) and warming	Additive or synergistic (most probable): Warming allows range expansion within lakes, including mussels into Lake Superior, increases potential Asian carp habitat and lamprey growth rates and fecundity; warmer winters allow subtropical invaders to survive. Antagonistic: Warming may create temperatures that are unfavorable for some invasives in shallow water or at southern limits in the Great Lakes.	Connecting channels, river mouths, shallow bays and nearshore in lower lakes
Climate change and habitat loss	Warming and wetland loss	Additive or synergistic (most probable): Warming may favor invasives such as *Phragmites* and decrease the amount of wetland area with native vegetation. Antagonistic: Warming without corresponding increases in precipitation may decrease water levels, increase growing season and potentially increase wetland area.	Urban areas and around river mouths with agricultural watersheds
Climate change and nutrients	Precipitation/ warming and phosphorus	Additive or synergistic (most probable): Warmer and longer summer seasons may favor more intense algal blooms, stratification, and hypoxia; more sediment P mobilization by longer and more widespread hypoxia; higher precipitation leading to increased river discharges may further increase loadings. Antagonistic: Warming may cause early algal blooms to consume available nutrients that would otherwise fuel blooms later in the season; warmer winters may result in less snowmelt for spring runoff and associated loading.	Eutrophic embayments and basins impacted by agricultural runoff
Nutrients and habitat loss	Phosphorus and wetland loss	Additive or synergistic (most probable): Less nutrient trapping by wetlands, and corresponding increase in impervious surface in filled urban wetland areas, increases lake loading; Higher nutrient loads in smaller wetlands may favor establishment and rapid growth of invasives (*Phragmites*). Antagonistic: In the absence of invasives, moderate increases in nutrient loading to coastal wetlands can enhance growth of native wetland vegetation, which can in turn trap more nutrients.	Urban areas and around river mouths with agricultural watersheds
Climate change and pathogens	Precipitation and fish pathogens	Additive or synergistic: Increase in intensity and frequency of rain events increases levels of pathogens delivered from watersheds; increase in beach closings and human health advisories (synergistic/additive). Antagonistic: Some pathogens such as VHS do not replicate or survive at higher temperatures.	Urban areas and at river mouths of agricultural watersheds with large numbers of livestock

* signifies a stressor pair selected for workshop discussion.

Toxic chemicals and nutrients

This potential interaction was a case study for workshop discussion, which focused on persistent, bioaccumulative and toxic (PBT) pollutants such as PCBs, and phosphorus. Studies have shown that increased productivity, which can be driven by increased phosphorus loading, can decrease the concentration of PBTs in higher trophic level organisms by biodilution (e.g., Berglund et al. 2001; Clayden et al. 2013; Kidd et al. 1999; Larsson et al. 1992). Hence, phosphorus load reductions potentially may result in higher toxic chemical concentrations in organisms due to lower growth rates and less biomass dilution. Pickhardt et al. (2002) provide evidence of a significant decline in the concentration of methyl-mercury in *Daphnia* with increased phosphorus inputs. In this case, the contaminant pool is diluted by several factors including a larger amount of biomass making up the base of the food web, more effective transport of contaminants to sediment via algae sinking (higher rates of sedimentation), and more efficient growth of fish from increased food abundance and/or food quality (Guildford et al. 2008). Nutrient increases can also lead to increased bacterial growth rates and enhanced bacterial degradation of PCBs.

Workshop discussants recognized a number of factors that may influence the expression of an interaction. There was strong consensus that—as reported in the literature—stressors vary temporally and spatially and thus their interactions do as well. In locations such as the western basin of Lake Erie and other shallow productive embayments, the mechanisms described above are relatively strong. In the east basin of Lake Erie, in contrast, lower prey fish biomass, predator growth rates and limited burial may provide less opportunity for biomass dilution. More generally, this mechanism may be less effective in mesotrophic and especially oligotrophic regions of the Great Lakes basin. Although the persistent nature of many toxic chemicals means that the chemicals are less influenced by temporal considerations, those come into play through life stage and migration considerations. For example, larval feeding by fish on diatoms may influence toxic chemical uptake, and seasonal temperature patterns can influence primary productivity, and fish metabolism and growth rates.

From a management perspective, discussants felt that this well-documented interaction between two stressors should not deter continued focus on phosphorus load reductions to Lake Erie. However, there is a need to carefully communicate and manage expectations of the implications of phosphorus load reductions on PBT trends. In addition, monitoring of these two stressors should be coordinated, and additional research may be needed to understand response times between phosphorus load reductions and trends of PBTs and other contaminants in fish tissue.

There may be circumstances where increased nutrients could increase the influence of toxic chemicals. For example, nutrient-induced hypoxia could enhance mobility and microbial transformation of some toxic substances (e.g., methylation of mercury), possibly increasing bioavailability. Overall, however, evidence indicates that the main relationship between toxic chemicals and nutrients is antagonistic. This is due to a number of potential mechanisms including increased organic matter burial due to higher productivity sorbing and sequestering toxic chemical in sediment, as well as biomass dilution due to higher growth rates in fish and other organisms.

Invasives and nutrients

Dreissenid mussels and phosphorus are among the most significant specific stressors in these categories. Mussels have dramatically changed the Great Lakes ecosystem. Mussels likely trap and retain phosphorus in nearshore areas, thereby increasing benthic nutrient levels in shallow-water locations (Hecky et al. 2004). As mussels increase water transparency and convert particulate phosphorus to soluble reactive phosphorus, they are also causing declines in offshore primary production and nutrient concentrations (Cha et al. 2011; Hecky et al. 2004; Stow et al. 2014). The long-term trend toward more intense oligotrophy in Lake Michigan, Lake Huron and Lake Ontario appears related to the reduction in phosphorus concentrations in offshore waters (Dove and Chapra, 2015). This low offshore productivity may be impacting the upper food web, where prey fish biomass has declined (Bunnell et al. 2014). Another study by the IJC's Science Advisory Board[4] notes that the roughly 20-year decline in Lake Michigan's prey fish biomass parallels the decline in spring total phosphorus concentration.

The interaction between mussels and phosphorus is complex, and the total offshore impacts of this nutrient trapping or 'shunting' is an active area of research. Quagga mussels are able to colonize soft sediments in deeper waters, which could represent a permanent trapping mechanism for phosphorus, termed the "mid-depth sink" hypothesis by Vanderploeg et al. (2010). The redistribution of bioavailable phosphorus to the nearshore benthos (Ozersky et al. 2009), along with increased water clarity and light penetration due to mussel filtration, has also contributed to the expansion of macroalgae, particularly filamentous *Cladophora*, in some nearshore areas of Lake Michigan, Lake Huron, eastern Lake Erie and Lake Ontario (Howell 2018). Selective consumption of diatoms versus cyanobacteria feeding by mussels may contribute to harmful algal blooms. The net long-term impact of nearshore changes driven by mussels on offshore nutrient delivery and primary productivity, and the subsequent impacts to fisheries is an area of active research in the Great Lakes.

Consideration of this stressor interaction as a workshop case study resulted in several relevant observations. Both seasonal and spatial aspects of the interaction, including the variable paths of river plumes in three dimensions, need further study to more fully understand interactions. Other factors that are important in understanding nutrient and mussel interactions are predation on mussels by round gobies, and mussel effects on water clarity and concentration of nutrients in sediments via pseudofeces production that promotes nuisance algae. In some lakes, specifically Michigan and Huron, the nearshore nutrient trap (or shunt) has led to significant oligotrophy in offshore regions. This has potentially impacted fisheries, whereby the limited productivity offshore leads to a reduction in fish biomass (Bunnell et al. 2014). Management of these

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[4] The Science Advisory Board's *Understanding Declining Productivity in the Offshore Regions of the Great Lakes* report can be accessed at ijc.org/en/sab.

stressors individually or together faces significant challenges. Lakewide control of mussels is infeasible and so local measures are needed. Efforts to reduce nutrient loading to nearshore areas must be weighed against offshore oligotrophication due to mussels and its impact on fish populations. Additional concerns include the proliferation of macroalgae due to benthic storage of nutrients and greater light penetration, food web impacts, invasive species impacts beyond mussels (e.g., round gobies), climate change influences on loading and impacts on the fishery and associated management decisions.

Discussants agreed that mussels and nutrients were among the most important stressors in many parts of the Great Lakes. It was also considered to be one of the most intensively studied, with overall data quality and strength of evidence sufficient to broadly characterize the nature of the stressor pair interaction, especially in offshore areas. There is a need to improve nearshore research and monitoring to understand important process questions and to track impacts of management actions on the interaction of mussels and nutrients, as well as their food web and fishery impacts. More sophisticated analysis of nutrient ratios, of phosphorus and nitrogen speciation, and of three dimensional and seasonal dynamics of nutrient delivery around river plumes were also identified as areas that need research and monitoring attention.

The interaction of nutrient loading and invasive mussels results in an enhancement of conditions for some species (nearshore macroalgae) and a degradation of conditions for others (offshore fish), which creates a complex management environment when nutrient load reductions are considered in some settings. As the proliferation of macroalgae and reductions in fish biomass are both considered negative impacts, nutrient loading and invasive mussels often are acting in an additive or synergistic fashion. However, stressors may have a counteracting influence in some locations, where nutrient-induced seasonal hypoxia limits mussel abundance (e.g., the central basin of Lake Erie), or cyanobacteria may interfere with dreissenid mussel reproduction (Boegehold et al. 2018). Additionally, mussel feeding may sequester nutrients in sediment, reducing productivity and harmful algal blooms, and the invasive *Phragmites* may also take up and trap nutrients in coastal areas.

Habitat loss and invasives

Many specific habitats, invasive species and locations could be examined to explore the nature of this type of stressor interaction in the Great Lakes. However, Great Lakes wetland degradation and loss is among the most important concerns. In this context, stressor interactions may involve invasive plants such as *Typha* and *Phragmites*, and habitat modification may be due to water level change and shoreline hardening. Interactions likely vary spatially, among lakes and between wetland types such as lacustrine and river mouth wetlands, open shorelines versus embayments, *et cetera*. Spatial variation strongly influences the context of any interaction between invasive species and habitat degradation. Wetland types vary spatially as do abundances of invasive species and extent of wetland loss. Both large-scale water level fluctuations (as influenced by lake hydrological fluctuations) and local water level influences, such as dikes and pumping, can affect managed wetland viability as do shoreline hardening and urbanization.

Shoreline slope and water level fluctuations influence available wetland habitat and the opportunity for wetlands to shift location.

Consideration of this stressor interaction as a workshop case study resulted in several relevant observations. Evaluating the strength of stressor interaction across different environments and scales was beyond workshop scope, but discussants did recognize there are many possible scenarios for wetland habitats affected by invasive plants and water level fluctuations, reinforcing the importance of spatial and temporal considerations, and the difficulty of generalizing. Discussants felt that the mechanisms by which invasive plants and water level change influence wetland habitats is well studied. Surveillance can be accomplished with existing methods for determining wetland plant composition using satellite data, assessing other community elements using biological surveys and tracking water levels at monitoring sites. However, new surveillance techniques may be needed, as well as novel and more effective control techniques for invasive plants.

Discussants also felt that management actions are reasonably well understood. Within the limits set by basinwide hydrologic variability, water level management can be accomplished by allowing or creating natural fluctuations. Invasive plants can be managed by mechanical removal, chemical treatment or burning. However, challenges to management exist, including addressing multiple interests (e.g., homeowner and shipping concerns) and the influence of basin-scale natural fluctuations.

Other examples of a possible interaction between invasive species and habitat deserve brief mention. By enhancing light penetration, mussels can promote growth of nuisance macroalgae, and this may be further enhanced by nutrient runoff in areas with decreased wetlands for nutrient trapping. Some invasives including gobies favor rocky rip rap shoreline habitat, and may benefit from wetland loss. Habitat loss resulting from wetland loss may detrimentally affect native plant species, thereby benefitting invasives.

Invasive species may exacerbate the overall harm resulting from degradation and loss of wetland habitat, and wetlands are further impacted by water level fluctuations and shoreline development. For example, *Phragmites* impact on wetlands is likely to be greatest where development impacts on wetlands are strongest and in southerly regions (Mazur et al. 2014). Wetland degradation and loss together with invasive species are expected to have an additive or synergistic impact on overall wetland habitat extent and quality. Antagonistic interactions between these specific stressors seem unlikely. However, it is important to consider context with respect to these two stressors, including the spatial and temporal variability of each individual stressor.

Toxic chemicals and habitat loss

The macrophyte assemblage of wetlands plays important roles in the biogeochemistry of contaminants (Weis and Weis, 2004). They actively take up elements into plant tissue, which can lead to the immobilization of particular contaminants (e.g., metals). For this reason wetlands are often considered ‘sinks’ and are frequently constructed to prevent pollutants from moving into nearby water bodies. However, anthropogenic activities, such as land clearing, drainage for agriculture and the filling of wetlands to permit coastal development, have resulted in the historical loss of Great Lakes wetlands (Trebitz et al. 2009). In contrast to these beneficial services, wetlands—particularly those rich in organic matter—are important sites of methylmercury production when mercury is converted to a potentially more toxic and bioaccumulative form (Selvendiran et al. 2008). Thus, wetlands can be sources of methylmercury production and export. A number of studies have identified wetlands as a sink for total mercury but a net source of methylmercury (Brahmstedt et al. 2019; Driscoll et al. 1998; Grigal et al. 2000).

This analysis suggests it is difficult to generalize the type of interaction between toxic chemicals and habitat loss. Wetland loss can result in a loss of capacity to remove and sequester contaminants, but as wetlands promote methylation of mercury, wetlands also can be a net source for methylmercury, illustrating an additive or synergistic interaction. Conversely, there may be cases where filling of coastal wetlands can cap toxic chemicals in industrial areas such as river mouths and harbors, in which case loss of wetlands can reduce contaminant availability illustrating a reversal or mitigative antagonism.

Toxic chemicals and climate change

The interaction of climate with POPs is complex, and climate warming may influence POPs in several ways. Climate change alters a number of environmental factors such as temperature, solar radiation, wind and precipitation that can also alter the fate, transport, distribution and effects of POPs (Balbus et al. 2013; Hooper et al. 2013). For example, warming climate may increase microbial decomposition and the subsequent release of POPs from bottom sediments, increasing bioavailability for uptake (Yediler and Jacobs, 1995); but in some cases it may increase the degradation of contaminants to less toxic, more easily degraded molecules. Further, altered biotransformation of contaminants may lead to more bioactive metabolites, although this is contaminant dependent. Warming temperatures may produce a minor reduction in POP exposure to aquatic biota because of enhanced partitioning from water to the atmosphere, but can also increase bioaccumulation potential (Noyes et al. 2009). Temperature can affect several key fish processes including consumption, growth and respiration. It can also affect other key bioaccumulation processes including environmental (changing concentrations in media) and dietary exposure (changing predator-prey relationships) (Gouin et al. 2013). Climate change also influences Great lakes fisheries through its impacts on habitat, especially through the influence of thermal habitat on different life stages (Collingsworth et al. 2017).

Ng and Gray (2011) forecasted the effects of climate change on bioaccumulation in three Great Lakes fish species that were adapted to three different thermal regimes. As expected, warmer temperatures tended to limit growth potential for cold water species, whereas cold water limited growth for the warm water species. The impact of climate warming on growth depended on both the winter lows and duration, and the summer highs, in combination with the species' thermal limits. In general, the strength of the interaction between climate and toxic chemicals may depend on more than just the exposure to the contaminant but also the susceptibility of the individual or population which is being exposed (Schiedek et al. 2007). In addition, with many Great Lakes species living at the edge of their thermal range, any additional climate enhanced exposures to toxic chemicals may further hinder the ability of organisms to acclimate to their environment (Noyes et al. 2009).

Warming temperatures promote higher growth in fishes, potentially increasing bioaccumulation, and enhance mobility and microbial transformation of some toxic chemicals (e.g., methylation of mercury), thus possibly increasing bioavailability. However, warming may also accelerate microbial degradation rates and annual duration of higher activity, impacting some organic pollutants. In addition to temperature, a number of climate variables (precipitation, ice and snow cover) can also alter the fate and behavior of toxic chemicals (Macdonald et al. 2005). The complexity of any interaction between climate and toxic chemicals is determined by abiotic processes as well as a wide range of potential biotic responses.

Invasives and fish harvest

Invasives can reduce native fish populations thereby further impacting fish harvest regulations. While lake trout historically have been subjected to overfishing, the invasive sea lamprey has also caused significant damage to this species (Elrod et al. 1995), and continued control of lampreys is critical to maintaining Great lakes fisheries (Zielinski et al. 2019). Though lampreys are among the best studied invasive species impacting Great Lakes fisheries, VHS is also a concern. First diagnosed in the Great Lakes as a cause for fish kills in 2005, VHS has since been detected across all lakes. While a wide range of fishes have been impacted by VHS, the susceptibility varies across species. For example, Kim and Faisal (2010) found that, in general, cool-water fish species (e.g., muskellunge, largemouth bass, yellow perch) are likely more susceptible to the virus than are cold-water salmonids. Muskellunge have historically been in decline within the Great Lakes, attributed to overharvest and environmental degradation (Farrell et al. 2007). In the St. Lawrence River from 2005 to 2008, a significant die-off of muskellunge occurred concomitant with an outbreak of VHS. Interestingly, another invader, the round goby, also increased during this time period. Both perturbations have been strongly correlated with a significant decline in muskellunge population (Farrell et al. 2017) and may represent a synergistic interaction.

Fish harvest can be impacted by a number of variables, including other stressors like invasives, climate change and habitat loss. Muskellunge are apex predators and a highly sought sports fish, subject to several stressors, and VHS likely exacerbates harm to this species via an additive or synergistic interaction. However, examples are known where an invader can improve a local fishery, (e.g., round gobies are an abundant prey for bass and trout) or lead to a reduction in fishing pressure (e.g., zebra mussels improved water clarity, supporting visual predators like Lake Ontario salmon). Still, synergistic interactions or additive effects are the most likely when considering overfishing and invasives.

Invasives and climate change

The interaction between multiple invasive species and warming from climate change has been a primary concern since the 1990s. Studies of the survival and growth of dreissenid mussels at different temperatures suggest that temperature increases will disadvantage mussels at lower latitudes, but more northern populations will benefit from predicted climatic change and may extend their range to appropriate habitats in higher latitudes (Thorp et al. 1998). While zebra and quagga mussels have successfully colonized most of the bottom waters in the Great Lakes, offshore Lake Superior remains relatively unimpacted (Environment and Climate Change Canada and US Environmental Protection Agency, 2017). Higher water temperatures could permit increases in the populations of zebra and quagga mussels within Lake Superior (Huff and Thomas, 2014; Moy et al. 2010), but lower levels of calcium remain a limiting factor for both species (Trebitz et al. 2019). Changing water chemistry can also be important and may actually reduce the competitive advantage of some invasives. For example, as pH lowers, the saturation state of two forms of calcium carbonate will decrease, which is more energetically costly for calcifying animals such as dreissenid mussels (Gregg et al. 2012).

Warming potentially will increase the range of available habitat to other invasive species of concern, including Asian carp and other warmwater fish (Mandrak 1989; Melles et al. 2015), and may increase lamprey growth rates and fecundity (Hansen et al. 2016). Kramer et al. (2017) recently mapped the suitability for potential invasive species in the Great Lakes. Suitability was higher in the lower lakes for the northern snakehead and golden mussel and increasing temperatures may further increase their potential for invasion. However, warming may also create temperatures that are unfavorable for some invasives in shallow water or at southern limits in the Great Lakes. For example, the invasive spiny waterflea prefers cooler waters and may be limited by increasing temperatures (Pagnucco et al. 2015).

In most cases, the addition of a warming climate to invasive species effects is likely to result in an expanded distribution of the invasive, resulting in an additive or synergistic relationship. Warming also is likely to increase growth rates and metabolism of invasive species. However, warming can also create temperatures that are unfavorable for some invaders, especially in shallow waters or at the southern limits in the Great Lakes, while expanding ranges to the north for cold-limited species.

Climate change and habitat loss

Wetlands may be at greater risk from invasives such as *Phragmites* under warmer temperatures and a longer growing season (Mazur et al. 2014), further decreasing coastal wetland area with native vegetation in the Great Lakes. Warming without corresponding increases in precipitation would lower water levels, increase growing season and potentially increase wetland area. The most opportunistic species, however, such as *Phragmites*, are likely to colonize bare sediment exposed during low water periods (lower edge) or shortly after high water periods (upper edge) more rapidly than native plants. This has been simulated for the St. Lawrence River wetlands (Tougas-Tellier et al. 2015) with potentially dire consequences for native wetlands. This also presents a challenge for wetland restoration. The tolerance of *Phragmites* for harsher and more variable conditions than many native wetland plants gives them an advantage under climatic conditions that are more extreme in terms of temperature, hydroperiod and other factors (Pagter et al. 2005). Coastal wetlands that may have become fragmented and isolated by alteration could become reconnected briefly by high or low water, or pumping and water diversion, allowing seeds and propagules of invasives to move to new areas while these climate-induced invasion pathways are open.

The analysis suggests that climate change and habitat loss interactions are usually synergistic or additive. In general, it is expected that climate change will further stress native wetlands in the Great Lakes by favoring the growth and spread of invasive species. More variable and extreme climate and water level conditions favor opportunistic invaders such as *Phragmites*, which may be able to colonize new habitats during brief intervals of favorable and extreme conditions, thereby decreasing the amount of wetland area with native vegetation. Warming without corresponding increases in precipitation would decrease water levels, increase growing season, and potentially increase wetland area, but also may create conditions favorable for invasives to replace native vegetation.

Climate change and nutrients

Harmful algae blooms, a widespread concern in some areas of the Great Lakes, are primarily driven by nutrient loadings. Given that this loading is a product of both river flow and nutrient concentrations in river water, climate change is predicted to have a significant impact into the future, and may already be responsible for recent increases in runoff. Increases in precipitation and runoff are likely to occur during periods characterized by intensive agricultural activities (e.g., tillage and application of fertilizer and manure in the spring), thus contributing to increased nutrient loadings. Extreme precipitation events increased from 1970 through 2010, closely matching an increase in overall dissolved reactive phosphorus loads to the Lake Erie watershed (Stow et al. 2015). The conclusion that climate change may intensify the negative impacts of eutrophication was also the finding of a national study of harmful algal blooms (Chapra et al. 2017). Warmer and longer summer seasons may favor more intense algal blooms, lake stratification and hypoxia; and longer and more widespread hypoxia may enhance phosphorus mobilization from sediments (Steinman and Spears, 2020). On the other hand, warming could cause early algal blooms to consume available nutrients that would otherwise fuel blooms later in the season, as in Lake Erie in 2018; warmer winters may result in less snowmelt for spring runoff and associated loading.

In general, it is expected that wetter springs, greater nutrient loading, and warmer and longer summer seasons will favor longer and stronger stratification, resulting in hypoxia, release of phosphorus from the sediment, and subsequently more intense algal blooms. However, antagonism is also plausible, for example with warmer winters resulting in less snowmelt and spring discharge, thereby reducing nutrient loads, or similarly reduced loads associated with warming-induced increased evapotranspiration from the watershed.

Nutrients and habitat loss

Wetland loss and nutrient loading may interact due to the role of wetlands in sequestering nutrients. A number of studies have shown that most wetlands retain sediment, nutrients and toxic contaminants or transform the nutrients and toxic chemicals into less bioavailable or less harmful forms. In particular, wetlands have a high capacity to retain nutrients (e.g., phosphorus), helping to limit excessive phosphorus concentrations in surface waters (Dunne et al. 2015; Zedler 2003). A recent review by Currie et al. (2017) examined the highly effective role of wetlands for phosphorus reduction in the Great Lakes. Phosphorus cycling in wetlands is complex, involving both inorganic and organic forms of phosphorus including the incorporation of phosphorus into plant biomass (Reddy and DeLaune, 2008), as well as sedimentation and accretion (Currie et al. 2017). Within Lake Erie, wetlands often act as partial sinks or transformers of nutrients and could be an important factor in mitigating eutrophication in the western basin of Lake Erie (Watson et al. 2016). However, the loss of wetlands mobilizes these nutrients back into the surface waters. A recent review by Land et al. (2016) examining 203 freshwater wetlands found that on average, new and/or restored wetlands significantly reduced the transport of nutrients (total phosphorus and total nitrogen) and could be an effective tool in counteracting eutrophication.

Wetland loss and increased nutrient loading are likely to interact in an additive or synergistic fashion, with negative impacts on both. The loss of nutrient trapping otherwise provided by wetlands can potentially lead to enhancement of harmful algal blooms and bottom hypoxia. Higher nutrient loads in remaining, smaller wetlands may favor establishment and rapid growth of invasives (*Phragmites*) at the expense of native plants. In addition, wetland loss may result in an increase in impervious surface area, enhancing runoff and transport of nutrients or contaminants. Antagonistic effects may occur, for example, if moderate increases in nutrient loading to coastal wetlands enhance growth of native wetland vegetation, which can in turn trap more nutrients. On balance, additive or synergistic effects seem most likely.

Climate change and pathogens

There is a strong connection between rain events and the amount of pollutants entering the Great Lakes via tributary runoff and conveyance infrastructure (Patz et al. 2008). A wetter future climate is likely to exacerbate delivery of pathogens and other contaminants via tributaries and storm drains. Urban stormwater and sewer overflows introduce significant contaminant loads each year and are considered major sources of impairment in the United States (Marsalek and Rochfort, 2004). Many of these contaminants have been linked to adverse public health effects including exposure to fecal indicator bacteria (e.g., *E. coli*), pesticides and viruses (Haile et al. 1999; Liu et al. 2006). Animal wastes from agricultural sources are another important source of pathogens in surface water. The impact of stressor interactions on human health was not a focus of this study, but the IJC Health Professionals Advisory Board commissioned a separate contractor study that examined this topic in more detail (LimnoTech 2019; McLellan et al. 2018). Elevated levels of bacteria are one of the most common causes of water quality impairments in the Great Lakes watersheds (US Environmental Protection Agency 2004). This is because stormwater contaminated with sewage can increase the levels of presence of human bacteria and viruses in surface waters (Dila et al. 2018). Within Great Lakes tributaries, storms have been shown to increase pathogens by several orders of magnitude (McLellan et al. 2018; Templar et al. 2016). While many of these pathogens die or are heavily diluted by the time they reach the open waters of the Great Lakes, Newton et al. (2013) tracked the contamination up to three kilometers offshore following heavy rains and up to eight kilometers offshore after a sewage overflows (Dila et al. 2018). Increases in heavy rainfall and warmer lake water are expected to contribute to increased contamination by overwhelming the combined sewer systems and increasing storm runoff.

The fish virus VHS may be an example where climate change is likely to reduce pathogenicity. As discussed earlier, most VHS outbreaks occur when water temperatures are 39°F to 57°F, and fish rarely die from VHS above 59°F. Whether a warming climate influences other pathogens is a future research need. With regard to pathogen delivery to Great Lakes receiving waters, an increase in storm events under future climate change is likely to be an additive or synergistic interaction, resulting in an increase in beach closings and human health advisories. While less common, antagonistic interactions may occur, as in the case of pathogens that do not survive at increased temperatures.

5.3 Spatial and temporal variability in stressor pair interaction

When considering interactions of stressors, an important factor to evaluate is the variation in their occurrence that dictates (1) the possibility of interactions, and (2) the intensity of their interactions; spatial and temporal variability are both important. A mapping of 34 individual stressors across the surface of the five Great Lakes revealed considerable spatial variability in stressor intensity between nearshore and offshore areas, between upper and lower lakes, and between individual stressors (Allan et al. 2013). For example, each invasive species has a species-specific distribution based on its habitat and other environmental requirements. Warming trends vary across the lakes separately from precipitation intensity and runoff, and these two climate variables have different seasonal effects (Bartolai et al. 2015; Mason et al. 2016). The greatest overlap of stressors is likely to be found in nearshore waters, near urban areas, and around river mouths (Allan et al. 2013; Host et al. 2019; Larson et al. 2013; Robertson et al. 2018). For example, increased precipitation leads to higher loadings of nutrients, pathogens and toxic chemicals at outlets of agricultural and urban watersheds, and where urban storm drains and combined sewer outfalls occur. Further, most nonpoint source loading occurs during large runoff events, which are more common during the spring and early summer.

Because individual stressors vary both temporally and spatially, their interactions will likely vary across both scales. It is reasonable to assume that many stressors would have the greatest opportunity to interact in nearshore areas and shallow embayments, such as Maumee Bay or Sandusky Bay in Lake Erie, with long water residence times and elevated summer temperatures (Salk et al. 2018; Verhamme et al. 2016). In addition, many stressor interactions, and potentially their impacts, could be seasonally amplified, whether by warm summer temperatures and lake stratification, by interaction with organisms during particular life cycle stages (e.g., nesting, spawning), or during vulnerable periods (e.g., end of winter, or during migration). Temporal coincidence of stressor occurrence and potential interactions could reasonably be expected to be greatest in spring and summer during periods of high river flow and high water temperature.

Table 2 provides an initial assessment of locations within the Great Lakes where each stressor pair is most or least likely to exhibit an interaction that may either enhance or offset the negative influence of one or both stressors. Note that research to demonstrate the reality or magnitude of these hypothesized interactions is lacking in most cases. Particular stressor pairs would be expected to manifest differently in each lake, and the within-lake patterns would reflect the spatial complexity of driver distribution. For example, the nearshore–offshore trend applies to both Lake Erie and Lake Superior, but because additive stress is much greater in Lake Erie (Allan et al. 2013) and the lake itself is smaller, the gradient is less distinguishable. These proposed interaction patterns may merit further research.

Temporal trends in priority stressors may also influence the potential for stressor interactions. Changes over time have been observed in many Great Lakes stressors, which, in turn, would be expected to influence their interactions as well. Many stressors have been stabilized or put into a declining state by human actions. Examples of mostly stable, declining, or prevented stressors include several invasive species (e.g., lamprey, mussels, Asian carp); fish overharvesting; point source and particulate phosphorus nutrient loading (but not dissolved phosphorus); pathogens in treated wastewater, combined stormwater overflows, and contaminated drinking water; wetland habitat destruction; and many measured toxic chemicals in sediment and biota. Stressors or undesirable conditions that may not fit the description of stable or declining include *Phragmites* occurrence, climate change, and dissolved phosphorus loading in some embayments, and emerging contaminants. Many of the stressors that are stable or declining require continuing investment to maintain that status (e.g., lamprey control) or to prevent the appearance of new stressors (e.g., new invasives), including ongoing investment in monitoring programs and in enhancement of policy frameworks, development of effective regulations, and synchronization of regulations across state, provincial, and international boundaries. Others stressors have declined but remain concerns; a full understanding of the rates and processes involved is lacking. This includes drivers of fish consumption advisories due to the presence of persistent organic pollutants (e.g., PCBs, polybrominated diphenyl ethers, PFAS) as well as mercury.

6.0 Conclusions: Management and Policy Implications of Stressor Interactions

6.1 Main findings: stressor interactions and cumulative stress

Stressor interactions in the Great Lakes are important to consider and are likely to result in an increase in cumulative ecosystem stress. Quantitative syntheses of multiple studies in freshwater systems generally, but not always, find that stressor interactions most frequently are synergistic or antagonistic rather than additive (**Figures 1** and **2** on page 4). Because antagonism includes cases where the combined effect of two stressors is less than their sum but greater than either stressor alone, cumulative stress from multiple stressors may often exceed the influence of the dominant stressor. As a consequence, many areas of the Great Lakes will experience cumulative stress from the presence of multiple, co-occurring stressors. However, even if individual stressor effects are well understood, cumulative stress is difficult to assess.

This report examined the most probable outcomes of pairwise stressor interactions for 11 stressor pairs involving the seven individual stressors considered amongst the most important and best understood stressors affecting the Great Lakes (**Table 2** on page 13). This assessment identified many examples where the harmful effects of one stressor could be enhanced or offset by a second stressor.

Examples of enhanced harm due to stressor interactions, including synergistic, antagonistic and additive effects, are reasonably common. Stimulation of harmful algal blooms by excess nutrients is likely to be enhanced under a warmer climate, which favors cyanobacteria, and a wetter climate, which increases nutrient export from rivers. Higher nutrient levels combined with increased water clarity favors expansion of *Cladophora*. Degradation of wetland habitat likely favors invasive plants including *Phragmites* and *Typha*, and loss of wetlands eliminates a pathway of contaminant and sediment sequestration. While combined stress is almost certainly greater than any one stressor alone, it is difficult to state *a priori* what type of interaction should be anticipated

Examples where one stressor can mitigate the negative impact of another can be identified for a number of stressor pairs, such that the combined effect of two stressors together is less than their sum. In some instances, it appears that a second stressor more than offsets (reverses) another. In productive ecosystems, a greater biomass of biota acts to dilute contaminant load per unit mass, such that moderately to highly productive ecosystems may experience greater biomass dilution (e.g., reduced contaminant tissue concentrations) in response to nutrient enrichment. The fish virus VHS, a Great Lakes invasive pathogen, is most harmful at cooler temperatures, and so warming temperatures may limit its impact. Wetlands are important sites for conversion of mercury to methylmercury, a potentially more toxic and bioaccumulative form; wetland loss reduces this process.

Spatial and temporal variability in the occurrence of individual stressors, and long-term trends in their intensity, are important contextual considerations in the evaluation of stressor interactions. Because the majority of stressors originate on land where agricultural and urban activities occur, the intensity of many stressors is likely to be greatest in nearshore waters, and decrease with distance from shore (**Table 2** on page 13). In addition, stressor frequency and duration as well as the sensitivity and vulnerability of the impacted resource value can vary with weather extremes, ecosystem conditions and drivers of human activity. In some cases, the analysis of interactions may be required at a relatively fine spatial scale. Trends in stressor interactions are likely linked to trends in stressors themselves, as well as the intensity of their management through time. For example, loading from point sources of toxic chemicals and nutrients has been substantially reduced over time, and invasive lampreys are effectively managed with lampricide application and other measures. Climate change, contaminants of emerging concern and many invasive species are not effectively managed.

6.2 Management implications

However, at this point in our understanding of stressor interactions in the Great Lakes, there is no clear resolution to the question of whether to continue traditional stressor-by-stressor management, or to adopt more holistic, integrated management of stressors within an explicit framework of interacting stressors. However, most of the research described previously suggests that stressor interactions can be important and through their influence, can both enhance and counteract the effect of one or both individual stressors. Therefore there may be an advantage to treating stressors more holistically in many cases, even if the exact nature of their interactions is unclear.

There are already some examples of existing Great Lakes' management programs that consider stressor interactions, and those examples may hold promise for improved understanding of stressor interactions. Multiple stressors are already being managed simultaneously for locations that have been designated as Areas of Concern under Annex 1 of the 2012 Great Lakes Water Quality Agreement, within a beneficial use or ecosystem services context that integrates stressors in terms of their ecosystem impacts. Multiple components of the Great Lakes fishery that interact are already carefully managed, including lamprey control, fish stocking and regulation of harvest seasons, species-specific fish quantity and size, and geographic location of harvest (e.g., Bunnell et al. 2014), with some explicit consideration of their interaction.

The type of interaction can inform prioritization of management actions. In the example where nutrient enrichment may promote biomass dilution of toxic chemicals, managers seeking to lower nutrient loads should be aware of the unintended consequence of higher toxic chemical burden per unit biomass in fishes. Management may focus on whichever is easiest to mitigate where two stressors acting together result in greater total stress.

Spatial variation in individual stressors and the environmental context of stressor interactions add complexity and uncertainty to management decisions. An approach appropriate to one location may not transfer easily to another.

The nonlinear nature of stressor interactions makes ‘tipping points’ difficult to anticipate. Recognition that ecosystem responses to both individual stressors and interacting stressors may be nonlinear (e.g., Horan et al. 2011) underlies the concern for ‘ecological surprises’ in which system decline may accelerate due to feedback loops, and reversal may be substantially more difficult (Bails et al. 2005).

6.3 Recommendations

1. That the Parties and other stakeholders that support Great Lakes monitoring and research programs investigate the gaps in understanding of stressor interactions described in this report, with an emphasis on those stressor interactions that are both most likely to impact natural environments across a range of environmental conditions and be amenable to management intervention at appropriate scales.

2. That any management actions in the Great Lakes by the Parties, state and provincial governments, and Tribes, First Nations and Métis governments should be targeted toward interactions that are best understood. Current management approaches that consider multiple stressors should be incorporated into approaches for addressing the interactions of other combinations of multiple stressors.

3. Lessons learned from science and management efforts that identify important stressor interactions should include spatial, temporal, and other contextual information that can provide critical information on transferability of information.

4. That the Parties tailor their Great Lakes science and management programs to explicitly consider how the multiple facets of climate change may interact with other stressors, and manage wherever possible toward enhancing resilience.

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Appendix: Workshop Attendance

Name	Organization
David Allan (Work Group Chair)	University of Michigan and IJC Science Advisory Board member
Tracie Baker	Wayne State University
Harvey Bootsma	University of Wisconsin - Milwaukee
Mary Anne Evans	United States Geological Survey
Kurt Fausch	Colorado State University
Lauren Fry	United States Army Corps of Engineers
Bob Hecky	University of Minnesota - Duluth and IJC Science Advisory Board member
Tomas Höök	Purdue University
John Jackson	Citizen activist and IJC Water Quality Board member
Lucinda Johnson	University of Minnesota - Duluth and IJC Science Advisory Board member
Donna Kashian (Day 2)	Wayne State University
Karen Kidd	McMaster University and IJC Science Advisory Board member
Marten Koops	Fisheries and Oceans Canada
Thomas Loch	Michigan State University
Mike McKay	University of Windsor
Carol Miller	Wayne State University and IJC Science Advisory Board Co-chair
Mike Murray	National Wildlife Federation and IJC Science Advisory Board member

Jeff Schaeffer	United States Geological Survey
Christina Semeniuk	University of Windsor and IJC Science Advisory Board member
Sigrid Smith	Delaware State University
Bob Sterner	University of Minnesota - Duluth
Craig Stow	National Oceanic and Atmospheric Administration
Don Uzarski	Central Michigan University
Matthew Child	IJC (Science Advisory Board - Science Priority Committee Secretary)
David Burden	IJC (Great Lakes Regional Office Director)
Ryan Graydon	IJC (Sea Grant Fellow)
John Bratton	LimnoTech (Contract Project Manager)
Jennifer Daley	LimnoTech (Contract Scientist)
Mike Donahue	AECOM (Contract Facilitator)