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3	Acting in the Face of Evidentiary Ambiguity, Bias, and Absence Arising from Systematic
4	Reviews in Applied Environmental Science
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21	Abstract: Evidence-based decision-making often depends on some form of a synthesis of
22	previous findings. There is growing recognition that systematic reviews, which incorporate a
23	critical appraisal of evidence, are the gold standard synthesis method in applied environmental
24	science. Yet, on a daily basis, environmental practitioners and decision-makers are forced to act
25	even if the evidence base to guide them is insufficient. For example, it is not uncommon for a
26	systematic review to conclude that an evidence base is large but of low reliability. There are also
27	instances where the evidence base is sparse (e.g., one or two empirical studies on a particular
28	taxa or intervention), and no additional evidence arises from a systematic review. In some cases,
29	the systematic review highlights considerable variability in the outcomes of primary studies,
30	which in turn generates ambiguity (e.g., potentially context specific). When the environmental
31	evidence base is ambiguous, biased, or lacking of new information, practitioners must still make
32	management decisions. Waiting for new, higher validity research to be conducted is often
33	unrealistic as many decisions are urgent. Here, we identify the circumstances that can lead to
34	ambiguity, bias, and the absence of additional evidence arising from systematic reviews and
35	provide practical guidance to resolve or handle these scenarios when encountered. Our
36	perspective attempts to highlight that, with evidence synthesis, there may be a need to balance
37	the spirit of evidence-based decision-making and the practical reality that management and
38	conservation decisions and action is often time sensitive.

Keywords: Environmental evidence, Evidence-based decision-making, Evidence synthesis,
Evidentiary uncertainty, Meta-analysis

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1. Introduction 43

From transitioning to a low carbon future (Hanley et al., 2018), to restoring degraded habitats 45 (Aronson and Alexander, 2013), or from bending the curve for biodiversity loss (Mace et al., 46 2018), to improving waste management in developing countries (Bartone and Bernstein, 1993), 47 "good" decisions need to be made that benefit the environment and humanity. Some issues and 48 decisions are local in scale (e.g., what to do at a given site in a particular region) while others are 49 national or global [e.g., United Nations (UN), Sustainable Development Goals (SDGs), 50 Conference of the Parties (COP), Intergovernmental Panel on Climate Change (IPCC), 51 International Union for Conservation of Nature (IUCN)]. In contemporary civil society, we 52 expect and even demand that environmental decisions are based on the best available evidence 53 (Sutherland et al., 2004). The concept of evidence-based decision-making is intuitive to 54 scientists, but there are many reasons why it can be difficult to achieve in practice (Head, 2010; 55 Oliver et al., 2014; Head, 2016).

56 A fundamental tenet of evidence-based decision-making is that there is some form of evidence

57 synthesis that collates evidence and identifies emergent patterns that guide decision-makers.

58 There are many forms of evidence synthesis (see Bilotta et al., 2015; Haddaway et al., 2015;

59 Pullin et al., 2016; Cook et al., 2017) but the gold standard, in many cases, is a systematic review

that leads to a quantitative meta-analysis. Systematic reviews differ from traditional literature 60

61 reviews in that they are repeatable, transparent, comprehensive (incorporating not just peer

62 reviewed findings but also relevant grey literature), and attempt to minimize bias through a

63 critical appraisal phase (see Table 1 for term definitions). Systematic reviews are particularly

64 attractive to decision makers when evidence from different sources conflicts, especially if accompanied by a quantitative synthesis that can weight the conflicting evidence according to 65 66 some measure of its reliability (e.g., the inverse of the effect size variance). Systematic reviews can also provide transparent and objective assessments where topics are controversial or high 67 profile e.g., environmental effects of pollution from mines or microplastics (Haddaway and 68 69 Pullin, 2014). For example, in health sciences, systematic reviews are widely embraced and 70 serve as the foundation for modern public health actions and medical interventions (see 71 Cochrane Collaboration; https://www.cochrane.org/; Lavis, 2009).

72 In an ideal world, environmental management decisions would be supported by a large amount 73 of evidence derived from robust studies with consistent findings, strong effect sizes and a strong, 74 universally applicable signal emerging from a quantitative meta-analysis. Yet, it is common for 75 systematic reviews to conclude that the evidence base is too small to enable meta-analysis (either 76 due to lack of studies or studies being excluded due to poor reporting -e.g., no variance or 77 sample sizes provided), or that the evidence base is of low reliability (e.g., biased in various 78 ways such as lacking controls, baseline data prior to intervention(s), inadequate sample sizes). 79 For example, Cook et al. (2014) investigated the contribution of systematic reviews to 80 environmental management and conservation decisions and found that, of the 43 they reviewed, 81 the strict eligibility criteria for reviews and the limited quality of much of the available primary 82 literature led to a median of only 12% of relevant studies being included in the meta-analysis. In 83 turn, these types of constraints can lead to results that are not robust (i.e., only a narrative analysis is possible), not generalizable (e.g., a different measure used by primary studies or 84 85 indirect response), and/or highly variable with respect to the meta-analytical results. Beyond

these limitations, the time, funding, and technical expertise required to conduct systematicreviews can be considerable.

88 In many ways, the outcome(s) of a systematic review depend entirely on the scientific rigour of 89 the available evidence base. Some forms of interventions and studies will never lack bias given 90 inherent limitations, particularly with respect to identifying appropriate controls or replicates in 91 natural systems. Indeed, demonstrating causal relationships between stressors and responses in 92 environmental systems is challenging because of the natural variability in environmental 93 responses and the difficulties associated with performing rigorous experiments [e.g., lack of 94 before-impact data, poor control matching, flawed units of replication (i.e., pseudoreplication), 95 an inability to randomize treatments, and the presence of uncontrolled confounding factors] 96 (Beyers, 1998; Downes et al., 2002; Norris et al., 2005, 2012; Nichols et al., 2017). These issues 97 weaken our ability to infer with confidence that any observed biological impairment is caused by 98 the suspected environmental stressor, or that an ecological recovery resulted from the 99 management intervention designed to mitigate the impairment (Downes et al., 2002). When a 100 systematic review results in an evidence base that is ambiguous, biased, or that provides little or 101 no additional evidence to help inform management decisions, authors tend to focus on 102 recommendations to improve the quality of primary research, which is unsatisfying and 103 unacceptable to most commissioners/funders. Here, we provide practical guidance for acting in 104 the face of evidence from systematic reviews that is ambiguous, biased, and/or absent.

105 2. Practical guidance

We acknowledge that there are many considerations taken into account prior to deciding on theuse of a systematic review in the decision-making process. Although these considerations are not

108 our focus, we think it would be helpful to first outline them below. Then, for the situation where 109 a systematic review is chosen as the appropriate tool, we provide guidance on what to do when 110 the evidence base for the systematic review leads to ambiguity, bias, or a lack of additional 111 information beyond what is already contained in the primary studies. This discussion piece was 112 not intended to act as a recipe guide *per se* to resolve or handle these scenarios when 113 encountered; rather, we outline potential options, providing a few specific examples where 114 possible and appropriate. Our focus was not on directly tackling the issue of how to implement 115 decisions when faced with evidence that is ambiguous, biased or when no additional evidence 116 arises. Instead, we aimed to describe the circumstances that lead to these issues and offer some guidance to navigate the decision-making process. 117

118 The first step in evidence-based decision-making is identifying the need for evidence relating to 119 a question of concern in policy or management. Often, questions stemming from discussions of 120 evidence needs start out very broad, and occasionally are not well defined (Game et al., 2013; 121 CEE, 2018). In some cases, the scale and scope of a problem may be such that it is obvious that 122 local data will be most important for making decisions. Therefore, constructing a clear, carefully 123 formulated question is essential. In this regard, there are a number of highly informative 124 resources available for guidance (e.g., Gregory et al., 2012; Groves and Game 2015; Hammon et 125 al., 2015; CEE, 2018).

Once the question has been properly formulated, the appropriate framework needs to be selected in a thoughtful way. To this end, there are also several useful tools for evidence-based decision making in environmental science. However, as noted by others (e.g., Pressey et al., 2013; Bower et al., 2018), deciding on which tool to use and how to implement it can be challenging for practitioners. Recently, four papers have provided guidance on how to address these challenges. 131 Schwartz et al. (2018) describe and contrast different planning and decision frameworks for 132 systematic decision making. Bower et al. (2018) provide guidance on how to choose among three 133 of the most common types of frameworks for solving environmental/conservation problems (i.e., 134 structured decision making, systematic prioritization, and evidence synthesis), and how to 135 identify less rigorous techniques when there are time or data availability constraints. Salafsky et 136 al. (2019) provide a typology of the different kinds of evidence a project team requires to help 137 make the various decisions needed to iteratively go through the decision-making process. 138 Finally, Wright et al. (2020) provide potential actionable steps for bridging the gap between 139 decision identification and action implementation (i.e., 'decision-implementation gap') as well as 140 avenues for future development of decision frameworks.

141 If it is decided that the question of interest requires a synthesis of previous findings (based on

142 guidance from sources such as those noted above), it is important to first check whether an

143 evidence synthesis already exists, such as a systematic review or map (e.g., Collaboration for

144 Environmental Evidence (CEE) syntheses library:

145 https://www.environmentalevidence.org/completed-reviews), a subject-wide evidence synthesis

146 [e.g., Sutherland et al. (2019); https://www.conservationevidence.com/], or a stand-alone meta-

147 analysis. If there is an existing evidence synthesis, one can make use of a new online, freely

148 available CEE evidence service known as CEEDER

149 (http://www.environmentalevidence.org/ceeder; Konno et al., 2020). With this database, one can

150 search evidence syntheses [commercially published reviews (available now) and grey literature

151 reviews (forthcoming)] on a specific question of environmental policy or management relevance,

and also obtain along with them an independent assessment of the reliability of each synthesis

153 with respect to its use in decision-making. However, if there is no pre-existing evidence

synthesis, or a more reliable or more up-to-date one is needed, then one must decide on theappropriate type of synthesis.

156 There are many approaches to evidence synthesis (described in Dicks et al., 2014; Bilotta et al., 157 2015; Haddaway et al., 2015; Pullin et al., 2016; Cook et al., 2017; Dicks et al., 2017; Sutherland 158 and Wordley, 2018). Previous authors have provided guidance on which approach to use 159 considering the type of question, policy context, desired outcomes of the synthesis (e.g., level of 160 certainty required, level of transparency/repeatability required) and constraints on decision-161 makers (e.g., the available funding, level of technical expertise, deadlines) (see Pullin et al., 162 2016; Cook et al., 2017; Dicks et al., 2017). Available approaches to evidence synthesis can be 163 viewed on an approximate continuum of very low rigor to very high rigor, and relatedly, limited 164 usefulness to very useful with respect to their ability to inform management decisions. As 165 mentioned previously, systematic reviews sit on that very high rigor end of the spectrum because 166 they incorporate mechanisms to minimize bias in searching, study inclusion, critical appraisal, 167 and meta-analytical sensitivity analyses, as well as increase transparency/reproducibility. 168 However, systematic reviews require considerable resources. For instance, Haddaway and 169 Westgate (2019) estimated that the average CEE systematic review takes 164 days at one full-170 time equivalent including vacations/holidays (but not weekends) and other regular disruptions 171 (standard deviation=23 days). Note that this average estimate represents resource requirements in 172 person days (i.e., the average number of days a project lead is working on the project) and not 173 the total time it would take for a systematic review project to be completed (i.e., including time 174 for journal assessment of the protocol and review), which - as identified by Haddaway and 175 Westgate (2019) – is approximately 737 days (standard deviation=364 days). Therefore, if 176 resource requirements go beyond the time (and/or budget) available to make a management

decision, one may want to consider a more rapid method of synthesis; however, this decision may come at a cost of lower confidence in synthesis results (see Cook et al., 2017 for a helpful decision tree). As noted by Cook et al. (2017), "The challenge is to select an approach that maximises the efficiency, appropriateness and effectiveness of the resources used in the review process to deliver conclusions, with a sufficient level of certainty for the decision context".

182 When a systematic review approach is deemed to be appropriate, there are still considerations 183 that must be addressed. For instance, at this stage, it is sometimes unclear what the evidence base 184 for the given topic actually resembles (i.e., Realistically how large is it? Is it generally reliable? 185 How broad or narrow is its scope and/or scale?), which can impact the decision of whether a 186 systematic review is in fact appropriate. If a systematic review proceeds, will there be sufficient, 187 unbiased evidence to make conclusions on management outcomes or will it only be able to 188 identify knowledge gaps and make recommendations on how to improve the validity of the 189 evidence base? Based on the guidelines set out by the CEE, early stages of a systematic review 190 involve a scoping exercise to develop the search string and test for search comprehensiveness 191 (see Conducting a Search in CEE, 2018). However, this initial scoping exercise does not always 192 provide a clear indication of how large or reliable the evidence base is - i.e., of the total number 193 of studies found, how many studies are actually relevant to the management question (either 194 directly and/or indirectly), nor does it provide insights as to the reliability of those primary 195 studies - i.e., of those that are relevant, how many are unbiased? Therefore, if a systematic 196 review is believed to be needed and if time/resources permit, we recommend doing a more 197 rigorous scoping exercise to get an estimate of the size and reliability (internal and external study 198 validity; refer to Table 1) of the evidence base. If the systematic review is commissioned by 199 decision-makers, this would ideally be a separate contract, before deciding on what

200 tool/framework is likely more appropriate to address the environmental management question. 201 Here, the scoping exercise would first involve following the full CEE guidelines for article 202 searches (see Conducting a Search in CEE, 2018). Then, using a subset of articles captured by 203 the search, including commercially published AND grey literature sources, articles can be 204 screened using pre-defined eligibility criteria (e.g., specific population or intervention of 205 interest), to identify relevant sources of evidence. From here, an estimate of the inclusion rate 206 can be made (i.e., of the number of articles in the subset, how many were deemed relevant), and 207 used to predict how many articles from the full search results could be relevant to the review. 208 Additionally, it is then possible to gauge the likely reliability of the full evidence base by estimating how many of those articles deemed relevant from the subset were found to be credible 209 210 (e.g., overall high, medium, low study validity) In doing so, one can get an approximate estimate 211 of the size and reliability of the evidence base, which can inform a decision as to the 212 appropriateness of a systematic review. To our knowledge, no one has previously suggested nor 213 attempted this form of a scoping exercise prior to conducting an evidence synthesis in 214 environmental science (providing an example using hypothetical data is beyond the scope of this 215 discussion piece). Assuming the evidence base is reliable, having an estimate of the size of the 216 evidence base will help shape expectations around timelines and costs for carrying out the full 217 systematic review.

Regardless of whether reliability of the evidence base is determined on the front-end with a
scoping exercise as suggested above or on the back-end of an ongoing or completed systematic
review, it is important for researchers to recognize five potential scenarios that will influence the
strength of the conclusions that are drawn from the systematic review. We describe these
scenarios directly below and paths forward when these scenarios are encountered:

i. If the evidence base is large, narrow in focus, and has relatively high reliability, the
conclusions drawn from the systematic review exercise should not be limited by issues of
evidentiary bias, or absence of additional evidence. However, there may be issues of
evidentiary ambiguity; in this case, see 2.1 What to do when the evidence base is *ambiguous*? below.

- ii. If the evidence base is large, narrow in focus, and has mixed reliability, the conclusions
 drawn from the systematic review exercise may be limited by evidentiary ambiguity
 and/or bias; in this case, see 2.1 What to do when the evidence base is ambiguous? AND
 2.2 What to do when the evidence base is biased? below.
- iii. If the evidence base is large, narrow in focus, and has generally low reliability, the
 conclusions drawn from the systematic review exercise will be primarily limited by
 evidentiary bias and a different framework/tool should be considered instead of a
 systematic review (see Cook et al., 2017; Bower et al., 2018) but also see 2.2 What to do
 when the evidence base is biased? below.
- iv. If the evidence base is deemed large but broad in scope/scale/outcome types, the
 conclusions drawn from the systematic review may be limited by evidentiary ambiguity.
- If this limitation is identified on the front-end of a systematic review, one can:
- a. Consider a systematic map as a starting point to generate a database and identify
 knowledge gaps (i.e., primary research needs) and clusters (i.e., areas for future
 systematic reviews) (see CEE, 2018).

243	i. The systematic map can also be combined with Multiple Expert Consultation +
244	Delphi method to analyze evidence over a broad area relatively quickly (Dicks
245	et al., 2017).
246	b. Consider narrowing the scope (e.g., select a clear knowledge cluster from scoping
247	effort and focus the systematic review on that topic).
248	If this limitation is identified during the systematic review process (i.e., back-end), see
249	2.1 What to do when the evidence base is ambiguous? below.
250	v. If the evidence base is sparse, the conclusions drawn from the systematic review will be
251	limited by the absence of additional information. If this limitation is identified on the
252	front-end of a systematic review (i.e., during the scoping exercise), one can:
253	a. Consider broadening the scope of the review to capture more evidence (e.g., multiple
254	forms of interventions and outcomes).
255	b. Consider broadening the review search to include openly accessible datasets to make
256	use of additional data from non-target studies that have attained relevant information
257	to address different research questions (see Culina et al., 2018).
258	c. Revisit other frameworks/tools (i.e., Multiple Expert Consultation + Delphi method)
259	(see Dicks et al., 2017 and Bower et al., 2018).
260	d. Proceed with the systematic review but acknowledge and communicate clearly with
261	practitioners the limitations of the current evidence base to manage expectations
262	(i.e., inform them that meta-analysis will not be possible and therefore, the synthesis

- will take the form of a narrative synthesis); in this case, see 2.3 What to do when
 there is no additional evidence? below.
- If this limitation is identified during the systematic review process (i.e., back-end), the conclusions drawn from the systematic review will also be limited by the absence of additional information; therefore, see 2.3 *What to do when there is no additional evidence?* below.

269 2.1 What to do when the evidence base is ambiguous?

270 In science, the term uncertainty is often treated as a single concept that simply represents the 271 absence of precise information (Molden and Higgins, 2004). However, important distinctions 272 have been made between different varieties of uncertainty. One such variety, ambiguous 273 uncertainty, is a term that is commonly used but is not easily defined. This is because scientists 274 sometimes use common words to mean different things but also different varieties of uncertainty 275 are not mutually exclusive. For instance, Molden and Higgins (2004) describe ambiguous 276 uncertainty as an abundance of conflicting information regarding a possible decision. Whereas 277 Smith and Stern (2011) describe ambiguity as being related to outcomes for which probability 278 statements cannot be provided (i.e., arising when there are impacts whose uncertainty one cannot quantify via probabilities; also known as Knightian uncertainty). They also acknowledge that 279 280 ambiguity sometimes reflects uncertainty in an estimated probability (i.e., imprecision 281 uncertainty). A key difference between these types of uncertainty is that the impacts of 282 imprecision uncertainty on decisions can be more easily explored via sensitivity analysis (e.g., 283 Tulloch et al., 2013). An important point noted by Smith and Stern (2011) is that, while science 284 aims to reduce ambiguity and quantify imprecision, there is not always a clear distinction

between the two. What matters in the context of evidence synthesis is that ambiguity arising
from the evidence base and results of a systematic review, whether due to quantifiable or
unquantifiable uncertainty, can translate into ambiguity in terms of the appropriate decision or
management response (Faucheux and Froger, 1995).

289 To address ambiguity arising from systematic reviews, we first encourage that researchers and 290 decision-makers embrace and accept the fact that decisions are almost never final, particularly at 291 large spatial scales (species extinctions are an obvious exception to this). Decisions are often 292 revisited, changed, or cancelled based on the accumulating evidence or its interpretation in 293 different socio-political frameworks. Furthermore, it may be necessary to acknowledge that some 294 decisions cause synergistic and some antagonistic responses given the complexity of biological 295 and human responses to change (e.g., Folt et al., 1999; Côté et al., 2016). To that end, it is 296 worthwhile establishing dynamic processes that re-evaluate evidence as new evidence becomes 297 available or contexts change (Gonzalez, 2005). We also encourage decision makers to consider 298 an adaptive management approach that incorporates or studies the outcome of a particular 299 management decision, which can be used to update the evidence base itself. Evidence synthesis 300 is best achieved when new evidence is incorporated into the evidence base as it becomes 301 available. Currently, there is no established CEE framework for this process; however, it is 302 common in the healthcare field and guidance has been developed in that realm (Moher and 303 Tsertsvadze, 2006; Garner et al., 2016; also see 3 Final remarks for suggestions for future work 304 below). This has become particularly salient during the COVID-19 pandemic where vast 305 amounts of new knowledge are being generated rapidly (Tricco et al., 2020), with lessons 306 emerging that are relevant to environmental evidence synthesis (Kadykalo et al., 2021).

307 In addition to incorporating new evidence as it becomes available, there are other ways of 308 exploring or reducing ambiguity in systematic reviews. For instance, it is common for an 309 evidence base to be mixed (i.e., having a blend of positive and negative evidence). Although 310 meta-analysis serves to combine these effects and obtain an estimate of the mean overall effect, 311 the variability around this mean can be high. Relationships between potential sources of 312 heterogeneity and effect size estimates can and should be explored as part of the meta-analysis. 313 However, these analyses are generally easier and more appropriate to undertake when there is a 314 large evidence base to reduce Type I (false positives) and II (false negatives) errors (CEE, 2018). 315 Furthermore, in some situations, the evidence base may contain broadly different outcomes, 316 management interventions, and/or taxa which could make studies inadequately comparable when 317 attempting to pool results in a meta-analysis. In these situations, heterogeneity and the potential 318 for ambiguity can be reduced by partitioning studies into more appropriately comparable 319 subgroups (e.g., different outcomes) and conducting distinct meta-analyses. Potential differences 320 in study characteristics can then be explored within these separate subgroups via the inclusion of 321 moderators.

322 Ambiguity may also arise as a result of the decisions made regarding how the meta-analysis was 323 conducted. As noted by Haddaway and Rytwinski (2018), each step in conducting a meta-324 analysis requires decisions that have both scientific and statistical implications. When meta-325 analyzing evidence, researchers are often faced with a number of decisions (e.g., choice of effect 326 size measure, variance calculations, model building, analysis software) and sometimes must 327 choose between equally valid approaches. Some of these meta-analytical decisions are 328 subjective, which can have implications on analysis results and lead to ambiguity. Therefore, it is 329 critical that researchers comprehensively and transparently report their methodology (i.e., what

330 decisions were made and why), and for journal editors and evidence synthesis coordinating 331 bodies (e.g., CEE) to ensure that quantitative synthesis methods are adequately reported and 332 justified in published systematic reviews. Furthermore, Haddaway and Rytwinski (2018) 333 advocate that, when possible, reviewers should attempt analyses in multiple ways if two or more 334 equally valid approaches are possible to see how results compare, presenting results within a 335 range of uncertainty when results conflict or differ. We acknowledge that regardless of whether 336 exploring ambiguity with moderator analyses or the meta-analytical choices made to summarize 337 the evidence, ambiguity may still remain. Therefore, we reiterate the importance of continuing to 338 incorporate new evidence as it becomes available, including new original research (e.g., on 339 additional sites or interventions) directed by the outcomes of ambiguous systematic reviews. To 340 do so requires that decision-maker and decision-making bodies are equipped to deal with 341 dynamic processes and willing to embrace the concept that most decisions are not final.

342 2.2 What to do when the evidence base is biased?

343 CEE (2018) defines bias (i.e., internal validity) as "a systematic deviation in study results from 344 their true value, i.e., either an underestimation or overestimation of the true value". Unlike 345 statistical uncertainty due to random error (present in all studies), bias as a result of a systematic 346 error cannot be overcome by increasing sample sizes in a given study or by combining study 347 results in a meta-analysis. If bias is present in primary studies, their results will be incorrect. 348 Subsequently, if a systematic review is based on incorrect evidence, the results of the meta-349 analysis will also be incorrect, resulting in misleading conclusions (Boutron et al., 2019). For 350 example, a misleading conclusion could stem from a systematic review where a precise but 351 wrong answer is made. Directly measuring bias within primary studies is challenging. Instead, 352 for systematic reviews, an indirect approach is used to infer the "risk of bias" by examining

aspects of research conduct (i.e., study design and methods) to determine whether studies used
adequate methodology to protect against bias (i.e., often referred to as critical appraisal of study
validity) (Higgins et al., 2011; CEE, 2018). To do so, researchers generally use review-specific
assessment criteria for appraising the interval validity – developed at the protocol stage and
ideally in consultation with topic experts and relevant stakeholders – categorizing studies, for
example, as having overall high, medium or low validity.

359 When the evidence base of a systematic review is assessed to have mixed reliability (i.e., the 360 evidence base is made up of both higher and lower risk of bias studies), it is important to 361 understand the potential impact of this bias on review results (Boutron et al., 2019). To do this, reviewers should test the influence of including studies of higher risk of bias on the review 362 363 results by means of sensitivity analysis. For example, if the evidence base allows for meta-364 analysis, one could stratify studies according to the overall risk of bias to produce and compare 365 multiple effect estimates from models that include, for example, all studies, studies at lower risk 366 of bias only, and studies at higher risk of bias only. Sensitivity analysis could be used to make 367 decisions as to whether (1) the meta-analysis should be restricted to studies at low risk of bias 368 when it seems clear from the model comparisons that the conclusions are likely impacted by the 369 inclusion of studies at high risk of bias, or (2) multiple effect estimates for different risk of bias 370 stratifications should be presented. The limitation associated with the former approach is the 371 potential for the loss of precision when excluding high risk of bias studies from the analysis (i.e., 372 not making full use of the evidence base). If there are relatively few studies with high risk of bias 373 but these studies have a clear impact on the mean effect estimate, excluding these few studies 374 would seem like a valid trade-off to achieve a result that is unbiased but potentially less precise. 375 However, if there are only a few studies at low risk of bias, excluding all studies with high risk

376 of bias may produce a result that is unbiased but imprecise, which may not be a valid trade-off. 377 In the latter approach (i.e., 2), while the impact of bias on review results is presented, the 378 limitation is reporting multiple effect estimates for a given outcome which may be confusing, 379 especially for decision-makers if they are looking for a single result. However, one option to 380 address this is to present a stratified (ordered) forest plot displaying all the information 381 transparently [e.g., a forest plot displaying the effect size estimates of each study included in the 382 meta-analysis stratified by the overall risk of bias judgment; see Fig. 1]. When the majority of 383 analyses trend towards the same conclusion, even if overall effect size estimates and significance 384 vary, this can provide greater support of decisions than a single overall quantitative estimate 385 from limited low risk of bias studies.

When the evidence base consists largely (or entirely) of low reliability studies, most often formal 386 387 meta-analytical procedures are not possible. In such cases, the evidence base is usually only 388 discussed narratively (i.e., tabulation and/or visualization). Although we have made a case that 389 systematic reviews conducted in accordance with international standards (CEE, 2018) are the 390 gold standard for evidence synthesis, the reality is that the existing literature base for some 391 environmental science topics are such that they will never be free of bias. Recognizing this, we 392 advocate, as others have done (e.g., Doerr et al., 2015), that researchers should strive to go 393 beyond a simple narrative synthesis and attempt some form of an analysis of the primary studies 394 even if formal rigorous meta-analytical methods are not possible [e.g., a sign test, meta-analyses 395 of p-values (see Borenstein et al., 2009); meta-analyses of single arm proportions for non-396 comparator studies (see Lipsey and Wilson, 2001), meta-analysis using an alternate effect size 397 metric such as percent change in intervention effectiveness (e.g., Rytwinski et al., 2019; see Box 398 1)]. A potentially less rigorous analysis with clear caveats and a discussion of the resultant

implications on the review findings will provide better, more usable information than no analysis
at all. However, if this path is chosen, it needs to be done acknowledging uncertainty and with
future efforts focused on improving and expanding the evidence base.

402 It is also important to recognize the fundamental importance of evaluating and synthesizing

403 evidence irrespective of whether a systematic review results in a quantitative analysis.

404 Systematic reviews generate a curated database of nearly all relevant evidence sources, which is

405 a highly valuable resource (e.g., Conservation Evidence;

406 <u>https://www.conservationevidence.com/</u>). Even when the evidence base as a whole is deemed to

407 be of low reliability, any and all evidence about the threat or role of interventions could help to

408 tip the scales in the direction of a good decision. Indeed, others have also advocated for

409 considering all forms of evidence appropriately when informing policy and practice (e.g.,

410 Sutherland and Wordley, 2018; Salafsky et al., 2019). The benefit of a systematic review, as

411 outlined above, is that study validity is assessed for each study such that if it is deemed of low

412 reliability, one is told why that is the case. In that sense, it is very much a "user be warned"

413 message. All this is to say that the database of existing studies when combined with detailed

414 information on study validity can play an important role in informing decisions.

415 2.3 What to do when there is no additional evidence?

In rare cases, systematic reviews may produce no additional evidence that can be used to address
a problem. Quoting the co-founder of CEE "evidence synthesis can't make sense out of nothing"
(A. Pullin, pers. comm.). Given the resource requirements for systematic reviews, this scenario
can be disappointing for both commissioners/funders and authors of the systematic review.

420 Ideally, it can be avoided by careful problem formulation (cf. Gregory et al., 2012; Bower et al.,

421 2018) to ensure the problem to be explored in the systematic review is clear and answerable.
422 Scoping exercises (outlined above) in the early stages of a systematic review also offer an
423 opportunity to identify questions for which no useful evidence is likely to be found. However,
424 the complexities of environmental decisions, whereby many components interact on different
425 spatiotemporal scales, mean that the problem of no additional relevant evidence may still arise
426 because little or no research has been conducted at a relevant spatial, temporal or taxonomic
427 resolution.

428 Such a situation may offer key opportunities since no additional evidence may still amount to 429 important additional information. First, it may indicate that the problem formulation process 430 should be re-visited to further refine the question toward something that is both relevant and 431 answerable. This outcome may not have been predictable at the onset of the project. Second, 432 finding no additional evidence may provide a strong mandate to act on current information, 433 despite uncertainties. Although environmental managers tend to be risk-averse (Tulloch et al., 434 2015), sometimes rapid action is crucial, despite high uncertainty (Martin et al., 2012). Finally, 435 no additional evidence may indicate that original field or lab research is necessary to address the 436 problem. In this case, additional tools can help focus the research on the spatiotemporal scales 437 that will inform management decisions. Value of information theory (Raiffa, 1968) is a powerful 438 tool to help focus research so that it is as informative for decisions as possible (Runge et al., 439 2011; Bennett et al., 2018). For example, Raymond et al. (2020) found that optimally locating 440 surveys for threatened plant species using value of information theory would allow managers to 441 protect more habitats with their limited resources. They also found that for many situations, 442 acting on current information was more efficient than gathering more evidence. Similarly, 443 Maxwell et al. (2015) used value of information theory to show that new data would have

444 negligible impact on management decisions for halting koala population declines. Bayesian 445 belief networks, which incorporate uncertainty into interactive models of systems, can also be 446 used to identify key areas of uncertainty that can most influence decisions (e.g., McCann et al., 447 2006; Howes et al., 2010). Bayesian belief networks can also incorporate many different forms 448 of data. For example, Smith et al. (2007) predicted suitable habitat for the Julia Creek Dunnart 449 (Sminthopsis douglasi), an endangered marsupial, using a Bayesian belief network that 450 incorporated expert elicitation regarding habitat use (for which there was little detailed 451 information), remotely-sensed proxies for key environmental variables, and confirmatory data 452 from fieldwork.

453 **3. Final remarks**

454 We acknowledge there are future guidance needs with respect to improving evidence syntheses 455 in environmental science. For instance, to date, there have been relatively few rigorous methods 456 proposed or developed to include different ways of knowing (e.g., stakeholder, practitioner or 457 Indigenous knowledge) in formal evidence-based decision-making processes. Fortunately, there 458 are many groups working in this space (see Berkes, 2009; Phillipson et al., 2012; Haddaway et 459 al., 2019) and there are huge dividends to be realized should we be able to figure out how to do 460 so (Hulme, 2010). Yet, it is important to acknowledge that decisions based on "evidence" often 461 fail to recognize that most knowledge holders do not present their work in either the grey or 462 peer-reviewed literature. This does not mean that those sources of knowledge are any less valid. 463 Indeed, in many cases they are the only or best source of knowledge. What is lacking from 464 current evidence synthesis approaches are mechanisms to formally bridge those ways of knowing 465 with other traditional western science methods while simultaneously accounting for bias in all ways of knowing. The "two-eyed seeing" approach, which briefly, encourages that we learn to 466

see from one eye with the best in the Indigenous ways of knowing, and from the other eye with
the best in the Western ways of knowing, and that we learn to use both these eyes together, for
the benefit of all, is one of the first practical approaches for doing so (Bartlett et al., 2012).
However, it has yet to be fully embraced or extended to include knowledge keepers or holders
beyond Indigenous Peoples.

472 Furthermore, there are currently no guidelines available to provide a rigorous, transparent, and 473 unbiased synthesis of the literature to address more urgent environmental management/policy 474 questions (i.e., 1-2 months). The shortest currently available well-defined methods take two or 475 more months (i.e., Quick Scoping Reviews or Rapid Evidence Assessments) and lie between 476 regular literature reviews and systematic reviews in terms of rigour of assessment (Collins et al., 477 2015). Therefore, guidelines for rapid synthesis approaches need further attention. In the 478 meantime, if policy makers need to rely on less rigorous methods of evidence synthesis (e.g., 479 regular literature reviews, vote counting), it is essential that they are accompanied with clear 480 caveats. Additionally, horizon scanning could be used so that evidence needs are anticipated in 481 advance (Sutherland et al., 2020).

Further exploration into incorporating frameworks endorsed by other fields should also be
considered. For example, health care sciences have adopted the GRADE approach (Grading of
Recommendations, Assessment, Development and Evaluation;

485 https://www.gradeworkinggroup.org/) to help move from the results of the systematic review to

486 making conclusions and presenting the evidence to decision makers via summaries of evidence.

487 Here, GRADE is used to rate the body of evidence at the outcome level rather than the study

488 level, to provide an overall GRADE certainty rating (i.e., high, moderate, low and/or very low)

489 to evaluate the strength of recommendations in order to assist decision makers. GRADE provides

490 a reproducible and transparent framework for grading the certainty of evidence and strength of
491 recommendations for medical science; how this system could be adapted to the environmental
492 science realm deserves further consideration.

493 Furthermore, as touched on above in the section on What to do when the evidence base is 494 ambiguous?, developing approaches to updating and incorporating new evidence into the 495 evidence base as it becomes available is important to ensure systematic review are not at risk of 496 inaccuracy (Shojania et al. 2007). One novel approach stemming from the healthcare field, that 497 goes beyond simply updating the evidence base, is the concept of a living systematic review 498 (Elliot et al., 2014). Elliot et al. (2017) describe a living systematic review in practice as the 499 "continual surveillance for new research evidence through ongoing or frequent searches and the inclusion of relevant new information into the review in a timely manner so that the findings of 500 501 the systematic review remain current". In contrast to standard review updating, living systematic 502 reviews include an explicit and *a priori* commitment to keeping the systematic review as current 503 as possible with a predetermined frequency of search and review (e.g., most current living 504 systematic review pilot projects aim to search most sources at least monthly and make the results 505 of these searches visible to end users within another month) (Elliot et al., 2017). Living guideline 506 recommendations, as well as guidance on statistical methods for updating meta-analyses have 507 been developed for the health care realm (see Elliot et al., 2017; Simmonds et al., 2017). 508 Therefore, how this approach could work and be modified in the environmental field deserves 509 further consideration, especially where (1) evidence for particular topics are emerging rapidly, 510 (2) current evidence is ambiguous, and (3) new search may change policy or practice. 511 Furthermore, how this approach could be maintained and supported long-term with respect to the 512 required continual application of (modest) resources also deserves further attention.

513 In conclusion, in environmental management and conservation, there are many cases where the 514 evidence base is of sufficiently high validity and size to accommodate systematic reviews and 515 where conclusions from systematic reviews have been instrumental in informing policy and 516 practice (see Haddaway and Pullin, 2014). However, the reality is that there are circumstances 517 when the evidence base is simply vague, limited in size/scope, and/or affected by (unavoidable) 518 biases. Here, we have provided practical guidance for how to resolve or handle circumstances 519 that can lead to ambiguity, bias, and the absence of additional evidence arising from systematic 520 reviews (summarized in Box 2). We hope this advice will reinforce the idea that systematic 521 reviews are part of a suite of decision tools, which can inform each other (cf. Bower et al., 2018), 522 and that ambiguous, biased or no additional evidence arising from a systematic review can still 523 be an important outcome for decisions. Our perspective attempts to highlight that, in some 524 situations, there is a need of a balance between the spirit of evidence-based decision making (i.e., 525 using only the most rigorous studies in evidence synthesis to inform decisions) and the practical 526 reality that rapid action is often crucial for environmental management and conservation (i.e., 527 using what evidence is available now while identifying and/or minimizing ambiguity, bias, and 528 the absence of additional evidence arising from systematic reviews). This perspective does not 529 however provide practical advice for decision makers on how to implement a decision when 530 faced with these circumstances, as this was beyond the scope of our discussion. We acknowledge 531 that filling such a gap with practical guidance (e.g., establishing frameworks, standardized 532 processes) would be vital for those tasked with making environmental management and 533 conservation decisions, and as such deserves immediate consideration.

534 CRediT authorship contribution statement

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812 Box 1. A case study using the Canadian context.

813 In Canada, efforts to conduct and utilize systematic reviews for environmental management and 814 conservation are still in their infancy. However, progress is ongoing. For example, institutions 815 within the Canadian government, such Parks Canada, Environment and Climate Change Canada, 816 and Fisheries and Oceans Canada (DFO), have recently begun integrating formal systematic 817 reviews into their decision-making processes following guidelines developed by the 818 Collaboration for Environmental Evidence (CEE) (2018). Highlighting one such case here, 819 DFO's Fish and Fish Habitat Protection Program (FFHPP) was seeking advice on best practices 820 in habitat restoration and information on the effectiveness of restoration practices in regions of 821 varying productivity and community compositions. To address this request, Taylor et al. (2019) 822 conducted a systematic review (including a quantitative synthesis using formal meta-analytical 823 methods) to assess the effectiveness of techniques currently used to create or enhance spawning 824 habitat for substrate-spawning fish in temperate regions. This systematic review was conducted 825 under the guidance of the CEE (2018), and as such allowed reviewers to identify the most 826 relevant, and reliable (minimally biased) sources of information on the review topic. However, while the evidence base on the topic was relatively large, following such rigorous guidelines 827 828 resulted in the exclusion of several studies from the systematic review because they were 829 considered to be relatively low validity sources (i.e., susceptible to bias and/or had inadequate 830 study designs). To gauge the amount of information gained from including available literature 831 initially excluded from the Taylor et al. (2019) systematic review, a second (non-systematic) 832 review (i.e., Rytwinski et al., 2019) was conducted to produce additional evidence for 833 consideration in the agency's formal science advisory process. These two documents formed the

bases for a resulting Science Advisory Report (DFO, 2020) to provide science advice to DFOmanagers.

836 For further context, the systematic review (i.e., Taylor et al., 2019) used formal meta-837 analysis techniques to calculate effect sizes for various spawning habitat interventions. These 838 effect sizes were based on the standardized mean difference between intervention and control 839 groups (in this case, represented as a statistic known as Hedges' g), with individual studies 840 weighted according to their standard error. To calculate such effect sizes, replication was 841 required in study designs [i.e., >1 waterbody receiving a creation or enhancement of spawning 842 habitat treatment and >1 waterbody not receiving the treatment, the control]. For the second 843 review, to be inclusive as possible (i.e., allow inclusion of data sets that either lacked replication 844 or that did not report variances or sample sizes for mean outcomes), Rytwinski et al. (2019) did 845 not use formal meta-analytical methods. Instead, for any data set that had quantitative data 846 [either a mean (number of replicates >1) or total count (n=1) for both the intervention and 847 comparator group], they calculated the percent change in intervention effectiveness. Percent 848 change is a more basic, less robust statistic not traditionally used in meta-analysis though it does 849 provide some useful information that was otherwise excluded from the systematic review. In so 850 doing, the number of data sets included in quantitative synthesis increased from 53 in the Taylor 851 et al. (2019) systematic review to 228 in the Rytwinski et al. (2019) review. Within both the 852 Rytwinski et al. (2019) review and the DFO (2020) report, comparisons between the two 853 quantitative analyses were made, highlighting the similarities and differences in review 854 conclusions (e.g., see Table 1 in DFO, 2020), but most importantly, both attempted to provide 855 informative evidence with clear considerations for review limitations and caveats with respect to 856 study validity. For instance, while the results from Rytwinski et al. (2019) supported the general

857	findings from the systematic review, one of the most notable observations was that by adding the
858	lower validity studies, there was evidence of increased uncertainty in the estimated effectiveness
859	relative to the systematic review. Yet, this report did allow for the inclusion of a greater diversity
860	of species and intervention types, leading to valuable products such as a curated database with a
861	critical appraisal of included studies. As such, we highlight this case study as an example of how
862	researchers can make use of the entire evidence base on a topic, attempting some form of
863	analysis of the primary studies to make use of the entire evidence base on a topic, and making
864	use of all review end products, so as long as this evidence is accompanied with appropriate
865	considerations for study validity.
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880 Box 2. Summary of recommendations.

881 At the front-end of a systematic review

Attempt a more rigorous scoping exercise that enables estimation of the size and reliability of the
evidence base to identify the potential for ambiguity, bias, and the absence of additional
information.

885 <u>To address *potential* ambiguity:</u>

- consider a systematic map as a starting point
- consider narrowing the scope of the review
- 888 <u>To address *potential* bias:</u>
- consider a different decision-making framework/tool
- 890 <u>To address *potential* absence of additional evidence:</u>
- consider broadening the scope of the review to capture more evidence
- consider broadening the review search to include openly accessible datasets to make use
 of additional data from non-target studies
- 894 revisit other frameworks/tools
- proceed with the systematic review but communicate clearly with practitioners the
 limitations of the current evidence base

897 <u>At the back-end of an on-going or completed systematic review</u>

- 898 <u>To address ambiguity:</u>
- incorporate new evidence as it becomes available
- 900 partition studies for pooling into comparable groupings (e.g., different outcomes) and
 901 conduct separate analyses
- 902 investigate potential sources of heterogeneity
- attempt meta-analyses in multiple ways if two or more equally valid approaches are
 possible to see how results compare, presenting results within a range of uncertainty
 when results differ substantially

906	To address bias:
907 908 909	• investigate the influence of bias on the effect estimates when the evidence base has mixed reliability, and attempt to balance precision (making use of the entire evidence base) with minimizing biased systematic review results
910 911 912 913 914	• go beyond a simple narrative synthesis and attempt some form of analysis with a discussion of caveats and limitations, or make full use of systematic review end products (i.e., database of relevant evidence sources combined with detailed information on study validity) to help inform decisions when the evidence base consists largely of low reliability studies.
915	To address no additional evidence arising for a systematic review:
916	• re-visit problem formulation
917	• accept that fast action may be crucial, despite high uncertainty
918 919 920 921	• make use of additional tools that can help focus original field or lab research on the spatiotemporal scales that will inform management decisions (e.g., value of information theory, Bayesian belief networks)
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Term	Description					
Systematic review process components						
Critical appraisal of study validity	An assessment of the comparative validity of the included studies requiring a number of decisions about the absolute and relative importance of different sources of bias and data validity elements common to environmental data (CEE, 2018). Ensures that all individual studies are objectively assessed for <i>internal validity</i> (reliability; is there potential for error and bias in the methodology employed to generate the study data) and <i>external validity</i> (generalisability; how transferable is the study to the context of the question). It can form a basis for the differential weighting of studies in later synthesis or partitioning of studies into subgroups for separate analyses (see <i>Critical appraisal of</i> <i>study validity</i> (<i>SRs</i>) in CEE, 2018).					
Eligibility criteria	A predefined list of inclusion conditions (specified at the protocol stage) that determine which of the primary research studies identified in the searches are relevant for answering the review question; applied at the eligibility screening step of a systematic review (or systematic map) (CEE, 2018).					
Decision-making fra	ameworks/tools*					
Meta-analysis	A statistical tool used to combine the numerical results from across multiple studies to provide estimates of the overall mean effect and the variability around this mean (Smith and Glass, 1977). Such quantitative synthesis of study findings increases the effective power of analyses relative to single studies, and allows researchers to investigate effect modifiers and sources of heterogeneity that could not be easily examined within single studies (Stewart, 2010).					
Multiple expert consultation with Delphi method	With the help of a coordination team or a facilitator, this method combines the knowledge of multiple, carefully selected experts into either quantitative or qualitative assessments, using a formal consensus on the question (described and reviewed by Mukherjee et al., 2016; Pullin et al., 2016; Dicks et al., 2017).					

930 Table 1. Terms and definitions used within this paper.

Structured A well-defined method for analyzing a decision by breaking it into decision components including the objectives, possible actions, and models linking actions to objectives. It relies on the integration of scientific information and stakeholder values to develop solution strategies, and as such, provides inclusion and transparency throughout the decisionmaking process (Bower et al., 2018). It is organized into clearly delineated steps that formulate the decision-making framework (see Gregory et al., 2012 for details on each step, and Dicks et al., 2017 and Schwartz et al., 2018 for details on framework functionality and comparisons).

Systematic Refers to a broad set of tools for quantitatively ranking conservation conservation actions to maximize outcomes given limited resources; all of these tools prioritization share a similar structure (Margules and Pressey, 2000). It is most suited to problems where options are chosen based on trade-offs among attributes that are quantified using consistent measurements across all units (see Bower et al., 2018; Schwartz et al., 2018).

Systematic A form of evidence synthesis that aims to provide an accurate map description of the evidence base relating to a particular question where methods are specified a priori in a protocol. Although procedurally similar to a systematic review, systematic maps do not aim to provide a quantitative or qualitative answer to a particular question, but instead, an overview of research that has been undertaken (Haddaway et al., 2016; James et al., 2016). Reviewers use predefined methods to minimize bias in the way the evidence is identified and selected. A descriptive overview of the evidence base is developed that could inform further research and synthesis (e.g., by revealing knowledge gaps and identifying more specific questions suitable for Systematic Review) (CEE, 2018).

SystematicA highly structured form of evidence synthesis where methods arereviewspecified a priori in a protocol. The goal of a systematic review is to
answer a specific question as precisely as possible in an unbiased way.
The process includes collating all relevant evidence and critical appraisal
of the included evidence. Reviewers use predefined methods to identify
risks of bias in the evidence itself, and to minimise bias in the way
evidence is identified and selected, and thus provide reliable findings
that could inform decision making. May include a quantitative synthesis
of the included evidence to improve precision (Pullin et al., 2016; CEE,
2018).

Issues arising from a systematic review

Evidentiary ambiguity	A form of uncertainty, whereby the uncertainty of the impact(s) cannot be quantified via probabilities; acknowledging that this sometimes also reflects quantifiable imprecision (another form of uncertainty). Therefore, for the purpose of this paper, we describe it as ambiguity arising from the evidence base and results of a systematic review, whether due to quantified or unquantifiable uncertainty, potentially making the appropriate decision or management response unclear because it can be understood in more than one way.					
Evidentiary bias	Bias as a result of a systematic error; a systematic deviation in study results from their true value (CEE, 2018). When a systematic review is based on biased evidence, the results of the quantitative synthesis of a systematic review will also be incorrect, leading to misleading conclusions.					
Absence of additional evidence	The absence of any <i>new</i> evidence arising from a systematic review (opposed to the absence of any evidence at all); acknowledging that no additional <i>evidence</i> may still amount to important additional <i>information</i> .					
*This is not a full lis	t of frameworks/tools for evidence-based decision-making in applied					
environmental science; listed here are terms/phrases that are referred to in this paper. For more						
comprehensive lists and descriptions/comparisons of decision-making frameworks/tools, see						
Dicks et al., 2014; B	ilotta et al., 2015; Haddaway et al., 2015; Pullin et al., 2016; Cook et al.,					
2017; Dicks et al., 20	017; Bower et al., 2018; Schwartz et al., 2018.					
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941 Fig. 1. An example of a stratified forest plot (using hypothetical data) displaying overall effect 942 size estimates of the intervention effect from meta-analyses (using a random effect model=RE) 943 based on: all studies regardless of risk of bias (top panel); only studies at high risk of bias i.e., 944 low validity studies (middle panel); and only studies at low risk of bias i.e., high validity studies 945 (bottom panel). In the example provided, although the relative magnitude of intervention 946 effectiveness appears to be influenced by study validity, with higher estimated mean increases in 947 outcomes for the analysis based on studies with lower susceptibility to bias (bottom panel), all 948 analyses trend towards the same conclusion (i.e., that there is an estimated positive effect of the 949 intervention regardless of whether lower validity studies are included).

Study	. E	ffect Estimate (95% CI)
Study 1	⊢	0.17 [-2.59, 2.92]
Study 2 Study 3		0.33 [-2.37, 3.04]
Study 3 Study 4	· · · · · · · · · · · · · · · · · · ·	0.70 [-1.87, 3.28] 0.33 [-2.37, 3.03]
Study 5		0.03 [-2.38, 2.44] 0.92 [-1.36, 3.20]
Study 6 Study 7	· · · · · · · · · · · · · · · · · · ·	3.20 [0.41, 5.99]
Study 8 ⊢		-1.10 [-3.53, 1.33]
Study 9 Study 10	⊢∓∎−−1 ⊢∓∎−−1	0.57 [-0.62, 1.76] 0.70 [-0.52, 1.92]
Study 11	H∎H	2.90 [2.42, 3.38]
Study 12 Study 13		-0.01 [-1.05, 1.04] 1.15 [0.15, 2.15]
Study 14	 ■	0.57 [-0.01, 1.15]
Study 15 Study 16	;⊢∎⊸₁	1.90 [0.73, 3.07] 1.03 [-0.30, 2.35]
Study 17	⊢	2.76 [0.95, 4.57]
Study 18 Study 19		2.82 [1.39, 4.25] 0.98 [0.52, 1.44]
Study 20		1.05 [-0.29, 2.38]
RE Model for all studies	*	1.16 [0.67, 1.65]
Study 1	<u>н н</u>	0.17 [-2.59, 2.92]
Study 2	⊢	0.33 [-2.37, 3.04]
Study 3	⊢	0.70 [-1.87, 3.28]
Study 4	⊢ I	0.33 [-2.37, 3.03]
Study 5	⊢ <u></u>	0.03 [-2.38, 2.44]
Study 6	⊢ ■i	0.92 [-1.36, 3.20]
Study 7	⊢ −−−−−	3.20 [0.41, 5.99]
Study 8 ⊢		-1.10 [-3.53, 1.33]
Study 9	⊢∎	0.57 [-0.62, 1.76]
Study 10	⊨∔∎⊷	0.70 [-0.52, 1.92]
RE Model for high risk only	′ •	0.58 [-0.04, 1.20]
Study 11	⊢∎⊣	2.90 [2.42, 3.38]
Study 12	⊢	-0.01 [-1.05, 1.04]
Study 13	⊢	1.15 [0.15, 2.15]
Study 14	⊨∎→	0.57 [-0.01, 1.15]
Study 15	⊢ −∎−−→	1.90 [0.73, 3.07]
Study 16	⊢	1.03 [-0.30, 2.35]
Study 17	·	2.76 [0.95, 4.57]
Study 18	⊧ ∎	→ 2.82 [1.39, 4.25]
Study 19	⊢∎⊣	0.98 [0.52, 1.44]
Study 20	⊢	1.05 [-0.29, 2.38]
RE Model for low risk only	*	1.46 [0.81, 2.10]
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-2	2 0 2 4	6
	Observed Outcome	e

