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1 **Innovation and forward-thinking are needed to improve traditional**
2 **synthesis methods: a response to Pescott & Stewart**

3

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23

24 **Abstract**

- 25 1. In Christie et al. (2019), we used simulations to quantitatively compare the bias of
26 commonly used study designs in ecology and conservation. Based on these simulations,
27 we proposed 'accuracy weights' as a potential way to account for study design validity in
28 meta-analytic weighting methods. Pescott & Stewart (2021) raised concerns that these
29 weights may not be generalisable and still lead to biased meta-estimates. Here we
30 respond to their concerns and demonstrate why developing alternative weighting
31 methods is key to the future of evidence synthesis.
- 32 2. We acknowledge that our simple simulation unfairly penalised Randomised Controlled
33 Trial (RCT) relative to Before-After Control-Impact (BACI) designs as we assumed that
34 the parallel trends assumption held for BACI designs. We point to an empirical follow-up
35 study in which we more fairly quantify differences in biases between different study
36 designs. However, we stand by our main findings that Before-After (BA), Control-Impact
37 (CI), and After designs are quantifiably more biased than BACI and RCT designs. We
38 also emphasise that our 'accuracy weighting' method was preliminary and welcome
39 future research to incorporate more dimensions of study quality.
- 40 3. We further show that over a decade of advances in quality effect modelling, which
41 Pescott & Stewart (2021) omit, highlights the importance of research such as ours in
42 better understanding how to quantitatively integrate data on study quality directly into
43 meta-analyses. We further argue that the traditional methods advocated for by Pescott &
44 Stewart (2021) (e.g., manual risk-of-bias assessments and inverse-variance weighting)
45 are subjective, wasteful, and potentially biased themselves. They also lack scalability for
46 use in large syntheses that keep up-to-date with the rapidly growing scientific literature.
- 47 4. *Synthesis and applications.* We suggest, contrary to Pescott & Stewart's narrative, that
48 moving towards alternative weighting methods is key to future-proofing evidence
49 synthesis through greater automation, flexibility, and updating to respond to decision-

50 makers needs – particularly in crisis disciplines in conservation science where
51 problematic biases and variability exist in study designs, contexts, and metrics used.
52 Whilst we must be cautious to avoid misinforming decision-makers, this should not stop
53 us investigating alternative weighting methods that integrate study quality data directly
54 into meta-analyses. To reliably and pragmatically inform decision-makers with science,
55 we need efficient, scalable, readily automated, and feasible methods to appraise and
56 weight studies to produce large-scale living syntheses of the future.

57

58 *Keywords: evidence synthesis, meta-analysis, dynamic meta-analysis, living reviews,*
59 *automation, quality effects modelling, meta-analyses, risk-of-bias, critical appraisal, bias*
60 *adjustment.*

61

62 **Introduction**

63

64 Pescott & Stewart (2021) outlined their concerns over an alternative method of weighting in
65 meta-analysis we proposed called “accuracy weights” in Christie et al. (2019). These weights
66 were derived from our simulation study that aimed to quantitatively compare the performance of
67 different experimental and observational study designs (Christie et al., 2019). Their two major
68 concerns were that our accuracy weights were not generalisable and that quality score
69 weightings, such as ours, may still lead to biased estimates in meta-analyses. Here we respond
70 to their concerns and discuss why we believe alternative methods of weighting are central to the
71 future of evidence synthesis.

72

73 **1. Accuracy weights need improving and combining with other quality measures**

74

75 As Pescott & Stewart suggest, we acknowledge that our simulation may have unfairly penalised
76 Randomised Controlled Trial (RCT) designs, depending on whether researchers in ecology and
77 conservation do take into account pre-impact sampling. However, in our experience, few
78 Randomised Controlled Trials in conservation take account of pre-impact baseline data; this is
79 supported by a recent study quantifying the use of different study designs in the environmental
80 and social sciences (Christie et al., 2020a). We acknowledge that we did not discuss more of
81 the shortcomings of Before-After Control-Impact (BACI) designs in terms of the bias that can be
82 introduced by violating the 'parallel trends' assumption (Dimick and Ryan, 2014; Underwood,
83 1991; Wauchope et al., 2020). Therefore, with respect to comparing BACI and RCT designs, we
84 acknowledge our simulation has limitations.

85

86 Nevertheless, our major motivation was to demonstrate the difference in study design
87 performance between simpler designs (e.g., Before-After (BA), Control-Impact (CI), and After
88 designs) and more rigorous designs (RCT and BACI). Thus, we intentionally made our
89 simulation relatively simple to engage a wide audience of researchers. We have since built on
90 our simulations in Christie et al. (2020a), which uses an empirical, model-based methodology to
91 quantify the differences in bias affecting different study designs using raw (rather than
92 simulated) data from a large number of within-study comparisons. This more fairly quantifies the
93 bias associated with RCT versus BACI designs by making fewer, more statistically defensible
94 assumptions about the 'true effect' (to estimate bias) and inherently accounts for the parallel
95 trends assumption that can bias BACI designs (Christie et al., 2020a).

96

97 Pescott & Stewart also suggest our simulation weights do not capture the full range of potential
98 sources of bias affecting study designs and advise that assessments of study quality should
99 closely scrutinise the details of specific studies being summarised (e.g., using manual risk-of-
100 bias assessments). In our study, we specifically acknowledged that our weights were relatively

101 simple and need to be built upon to incorporate a wider range of study quality indicators; we
102 outlined possible approaches in the future that could integrate scores from critical appraisal
103 tools that exist for ecology and conservation (Mupepele et al., 2016). We are happy to see that
104 others are building on our work and investigating the use of a broader set of quality or validity
105 measures to weight studies in meta-analyses (e.g., Schafft et al. 2021, Mupepele et al. 2021). In
106 the next sections, we address Pescott & Stewart's criticisms of weighting by quality scores and
107 discuss statistical advances in applying quality score weightings to meta-analyses. We also
108 discuss the problems associated with the traditional methods advocated for by Pescott &
109 Stewart (such as inverse-variance weighting and manual risk-of-bias assessments).

110

111 **2. Recent advances in directly integrating data on study quality into meta-** 112 **analyses**

113

114 In Pescott & Stewart's discussion on why they advocate against weighting by quality scores in
115 meta-analyses, they omit over a decade of research in epidemiology on alternative quality score
116 weighting methods that have overcome many of the problems they discuss (Doi, Barendregt
117 and Mozurkewich, 2011; Doi et al., 2015a, 2015b; Doi and Thalib, 2008; Rhodes et al., 2020;
118 Stone et al., 2020). In particular, 'bias adjustment' methods, such as quality effects models,
119 represent an active and promising area of research in evidence synthesis in epidemiology (Doi,
120 Barendregt and Mozurkewich, 2011; Doi and Thalib, 2008; Rhodes et al., 2020; Stone et al.,
121 2020).

122

123 Critical appraisal is traditionally used to descriptively report the risk of bias for different studies,
124 rather than trying to quantitatively incorporate those assessments within the analyses
125 themselves (Johnson, Low and MacDonald, 2015). Instead, our accuracy weights are related to

126 the field of 'bias-adjustment' methods which seek to directly integrate risk-of-bias assessments
127 into meta-analytic results (Stone et al., 2020). Criticisms of quality score weightings have
128 centered around four major issues: 1.) the choice of quality scale influences the weight of
129 individual studies; 2.) the meta-estimate and its confidence interval depends on the scale; 3.)
130 there is no reason why study quality should modify the precision of estimates; and 4.) poor
131 studies are not excluded (Stone et al., 2020). Therefore, as Pescott & Stewart also appear to
132 argue, any bias associated with poor quality studies can only be reduced at best, and not
133 removed (Stone et al., 2020).

134

135 Whilst proponents of quality score approaches accepted these criticisms and ceased their
136 development, an alternative, improved methodology called 'quality effects models' have
137 subsequently been developed and refined in recent years. This approach uses a relative scale
138 and 'synthetic weights' (yielding relative credibility ranks for different studies) that overcame the
139 major issues that affected quality score approaches, and has been shown to yield an estimator
140 with superior error and coverage to conventional estimators (Doi et al., 2015b, 2017). There are
141 a range of possible ways, each with advantages or disadvantages, to derive the relative
142 credibility weights for studies using numerical data generated by expert opinion (Turner et al.,
143 2009), data-based distributions, or statistically combining expert opinion and data-based
144 distributions (Rhodes et al., 2020). Therefore, results from further refining and improving our
145 simulations and empirical analyses (Christie et al., 2019; Christie et al., 2020a) could provide
146 valuable contributions to the active development of these methods to integrate data on study
147 quality directly into meta-analyses.

148

149 Pescott & Stewart focus on the possibility of incorporating study quality scores into meta-
150 regression approaches. Their criticism of our weights in their current form is that they are too
151 unidimensional and not study-specific; this is a criticism that we partially accept. Indeed, we

152 specifically discussed the need to expand and improve our weights to integrate other aspects of
153 study quality (e.g., using expert opinion, data-based distributions, or critical appraisal tools to
154 adjust relative credibility ranks; Rhodes et al., 2020). In hindsight, we should have dedicated
155 more attention to how we would further develop and more robustly apply our accuracy weights
156 alongside discussing advances in quality effects models.

157
158 Pescott & Stewart also suggest that we ignore issues relating to external validity. Given that
159 traditional weightings, such as sample size or inverse variance, also fail to consider external
160 validity, we find this an odd criticism, particularly given our simulation was clearly focused on
161 addressing issues of study design quality and internal validity. We are in fact developing an
162 alternative meta-analytic method, dynamic meta-analysis (Shackelford et al., 2021), based on
163 the Metadataset platform (www.metadataset.com), which we plan to use to test different
164 weighting methods, including 'recalibration' from the medical sciences (Kneale et al., 2019)
165 which aims to adjust studies' influence in meta-analyses based on their external validity (or
166 relevance to decision-makers). Again this work is in the early stages of development and there
167 are many methodological challenges to overcome, particularly in how to integrate 'recalibration'
168 methods into random effects models and how to ensure such interactive meta-analytic tools are
169 used robustly (Shackelford et al. 2021). Therefore, as Pescott & Stewart suggest, we believe it
170 should be possible to integrate internal validity or quality items, and external validity items, into a
171 hierarchical meta-regression framework, or to directly weight studies using new advances in
172 quality effects models as discussed previously (see Stone et al. 2020 for a comparison and
173 discussion of different approaches).

174

175

176 **3. Integrating data on study quality into meta-analyses is essential to the future of**
177 **evidence synthesis**

178

179 We also believe Pescott & Stewart's discussion presents a narrow vision of the challenges
180 faced by traditional critical appraisal and weighting methods. We believe that the traditional
181 'medical-style' approaches (e.g., manual risk-of-bias assessments combined with inverse-
182 variance weighting) that Pescott & Stewart believe should be adhered to are ultimately
183 inefficient and wasteful. The field of evidence synthesis is advancing at pace to respond to the
184 challenges of rapidly growing evidence bases and fast-moving crises, which requires new
185 methodologies that help to keep evidence bases 'up-to-date' or 'living', cost-efficient by working
186 at massive discipline-wide scales, and dynamically adjustable to be relevant to different
187 decision-makers' needs. Here we elaborate on why this is problematic to Pescott & Stewart's
188 assertion that we should continue to rely on traditional methods, rather than alternative
189 weighting methods such as the one we proposed in Christie et al. (2019).

190

191 **3.a. Alternative weighting methods facilitate more efficient, automated, living, large-scale**
192 **syntheses**

193

194 First, there is growing recognition that decision makers need constantly updated evidence
195 syntheses (Elliot et al., 2021) and that traditional synthesis methods (e.g., traditional systematic
196 reviews) are often too time-consuming, quickly go out-of-date, and can miss important
197 opportunities to influence practice and policy (Boutron et al., 2020; Grainger et al., 2019;
198 Haddaway and Westgate, 2019; Koricheva and Kulinskaya, 2019; Nakagawa et al., 2020;
199 Pattanittum et al., 2012; Shojania et al., 2007). Given that the scientific literature in most
200 disciplines is growing rapidly (Bornmann and Mutz, 2015; Larsen and von Ins, 2010) and that

201 publication delays already hamper evidence-based decision-making in crisis disciplines, such as
202 conservation (Christie et al. 2021), evidence synthesis needs to be as time- and cost-efficient as
203 possible (Grainger et al., 2019; Nakagawa et al., 2020). Generating large-scale, easily
204 updateable, 'living' evidence databases containing results and metadata of scientific studies
205 across subjects is therefore central to future-proofing evidence synthesis (Elliot et al., 2021;
206 Shackelford et al. 2019). It is these forward-thinking approaches to synthesis that can be
207 facilitated by alternative methods of weighting, which can use the metadata on studies to
208 automatically and rapidly critically appraise studies and weight meta-analyses, without the need
209 for cumbersome, inefficient, and ultimately subjective manual risk-of-bias assessments that
210 Pescott & Stewart promote. Inverse-variance or sample size weighting could equally draw on
211 these evidence databases, but are far poorer at capturing information on study validity (since
212 our simulation study showed that certain study designs may have lower variance but higher bias
213 (e.g., BA or CI) than other designs (e.g., RCT and BACI)).

214

215 Therefore, whilst we acknowledge Pescott & Stewart's belief that traditional methods to critical
216 appraisal (e.g., manual risk-of-bias assessments) are a key part of the rigour of current
217 evidence synthesis, we argue that such methods are not efficient, scalable, or feasible enough
218 for use in living synthesis projects that we need to deliver at scale to more comprehensively
219 bridge the research-practice and policy gaps (e.g., Conservation Evidence produced using the
220 subject-wide evidence synthesis methodology; Sutherland et al. 2019). We instead suggest that
221 more efficient alternative weighting methods to rapidly critically appraise and weight studies by
222 their validity and quality (e.g., through automating risk-of-bias assessments; Marshall et al.
223 2015) are urgently needed to ensure evidence synthesis can keep pace with the rapidly growing
224 scientific literature (Marshall and Wallace, 2019; O'Connor et al., 2018; Thomas et al., 2017;
225 Wallace et al., 2014). Increasingly using automated and data-based methods for estimating
226 different dimensions of study quality will become a more important and necessary approach to

227 speed up evidence synthesis (Marshall et al., 2020; Marshall, Kuiper and Wallace, 2015;
228 Marshall and Wallace, 2019; O'Connor et al., 2018; Tsafnat et al., 2013; Wallace et al., 2014).
229 Of course, it is important that automated methods, particularly for critical appraisal and
230 weighting, balance increased efficiency against high standards and rigour to ensure they give a
231 reliable reflection of the quality of studies – which we believe should act as a major motivation
232 for follow-up research to improve and expand upon our weights.

233

234 We also argue that the traditional method of descriptively reporting the risk of bias for different
235 studies in critical appraisal that Pescott & Stewart advocate for (rather than trying to
236 quantitatively incorporate this information within the analyses themselves) represents an
237 inefficient and wasteful use of this detailed information given the major investment of resources
238 they require (Johnson, Low and MacDonald, 2015; Haddaway and Westgate, 2019). Guidance
239 by the Cochrane Collaboration for medical syntheses currently makes risk-of-bias assessments
240 mandatory, but there is still no consensus on how to use them to 'adjust' the results of evidence
241 syntheses (Rhodes et al., 2020). The GRADE approach used in medicine, which Pescott &
242 Stewart appear to support, is to use risk-of-bias assessments to define a threshold beyond
243 which a recommendation can be supported, and then use subjective risk-of-bias assessment to
244 determine which side the true effect lies of a particular threshold (or within a certain range)
245 (Stone et al., 2020). This stratification of results (or regression models using risk of bias) has
246 been criticised based on empirical evidence suggesting that conditioning on risk of bias may
247 induce collider-stratification bias (Stone et al., 2019).

248

249 **3.b. Alternative weighting methods facilitate considering study quality as a spectrum**
250 **rather than a cut-off**

251 Another concern we have with the manual risk-of-bias assessments that Pescott & Stewart
252 advocate for is that these can be used to exclude studies from meta-analyses, which can have a

253 major impact in disciplines where evidence bases often lack more rigorous study designs, such
254 as conservation science (Christie et al., 2020b, 2020c, 2020a; Junker et al., 2020). Whilst this
255 may be justifiable in cases where studies are clearly extremely flawed or unreliable, we believe
256 the ‘rubbish in, rubbish out’ concept and idealised ‘best evidence’ approach (Slavin, 1986, 1995;
257 Tugwell and Haynes, 2006) is dangerous and ignores the fact that studies of lower quality can
258 add useful information to evidence syntheses (Davies and Gray, 2015; Gough and White, 2018;
259 Lortie et al., 2015). Rather than excluding studies judged to be of lower quality, we believe that
260 they should instead be included but treated with appropriate caution and uncertainty (Christie et
261 al., 2020a). We need new, alternative methods of weighting in meta-analyses to do this because
262 traditional inverse-variance weighting does not account for potential differences in bias
263 introduced by different studies (hence the previous reliance on excluding studies below an
264 arbitrary quality threshold; Doi and Thalib, 2008; Rhodes et al., 2018, 2020; Stone et al., 2020).
265 Pescott & Stewart’s assertion that we should not stray from weighting by inverse-variance also
266 ignores the fact that this traditional method is prone to bias when analysing both Hedges’ *d*
267 (Hamman et al., 2018) and log-response ratios (Doncaster and Spake, 2018; Bakbergenuly,
268 Hoaglin and Kulinskaya, 2020), which are two of the most commonly used effect size measures
269 in ecology and conservation.

270

271 The alternative weighting methods that we are advocating for do not enforce a cut-off threshold
272 in the evidence being used, but instead focus on weighting evidence on a spectrum of quality or
273 validity, which we believe is a more defensible philosophical approach – i.e., placing greater
274 weight behind studies that are more trustworthy and reliable. Furthermore, the approach of
275 excluding studies via risk-of-bias assessments has been criticised because resulting
276 recommendations from syntheses may rely on a small subset of studies (subjectively judged to
277 be of sufficient quality), which may be less robust than analysing a much larger set of studies
278 with variable quality (Davies and Gray, 2015; Gough and White, 2018; Lortie et al., 2015).

279 Indeed, during the Covid-19 pandemic, the overreliance of evidence-based recommendations
280 on Randomised Controlled Trials has been criticised for delays in promoting wearing of face
281 masks and coverings in Western countries, particularly when high quality non-RCT evidence
282 was available from community settings (The Royal Society, 2020). Pescott & Stewart's
283 comment: "Even studies that appear to be high quality may still contain non-obvious biases, and
284 apparently lower quality studies could in fact be unbiased for the effect of interest" surely
285 justifies why excluding studies using manual, subjective risk-of-bias assessments can be
286 dangerous – and why alternative weighting methods that consider a wide range of more
287 objective data and statistics on study quality are needed. Excluding studies based on manual
288 risk-of-bias assessments is also likely to strongly limit the scope, relevance, and external validity
289 of any recommendations made by evidence syntheses in crisis disciplines with patchy evidence
290 bases, such as conservation (Christie et al., 2020b; Gutzat and Dormann, 2020). Conversely,
291 alternative weighting methods would maximise the number of studies (and study contexts)
292 considered (whilst directly accounting for study quality), which is likely to be more useful and
293 efficient for informing rapid evidence-based decision-making in multiple different contexts.

294

295 Alternative weighting methods also facilitate the use of weighting by external validity (i.e.,
296 relevance), in addition to internal validity (i.e., reliability), as different components of the overall
297 validity of a study can be considered. As discussed earlier, the alternative weighting method of
298 'recalibration' has been proposed in the medical sciences (Kneale et al., 2019) to adjust studies
299 weights in meta-analyses by their relevance to a decision-maker's question and context of
300 interest (as trialled in dynamic meta-analyses on the Metadataset platform for interventions on
301 invasive species and agricultural management; Shackelford et al. 2019). The issue of external
302 validity and relevance is a crucial issue for decision-makers and the usefulness of evidence
303 syntheses, particularly in disciplines like ecology and conservation science where variation
304 between studies based on their local context (e.g., biophysical environment, species studied,

305 details of intervention carried out) is perceived to be large and important for management.
306 Traditional methods of synthesis advocated for by Pescott & Stewart typically fail to account for
307 or consider the relevance of different studies to decision-makers in any detail, and certainly do
308 not directly integrate this meta-analytic weightings of studies. As different studies will have
309 different levels of relevance to different decision-makers, these alternative weighting methods
310 also support the movement towards more interactive, living meta-analytic platforms for evidence
311 synthesis (rather than static publications of meta-analyses) that can be dynamically adjusted to
312 give bespoke evidence-based recommendations (Shackelford et al. 2019; Kneale et al. 2019).
313 Developing alternative weighting methods, rather than avoiding them, is therefore central to
314 increasing the usefulness and relevance of evidence syntheses to decision-makers.

315

316 **Conclusion**

317 We agree with Pescott & Stewart that synthesising the results of studies using different designs
318 is a fundamental issue for evidence synthesis – hence the urgent need for further scientific
319 investigation into how to directly integrate measures of study quality into meta-analyses
320 (Boutron et al., 2020; Hamman et al., 2018; Jenicek, 1989; Nakagawa et al., 2020; Sutherland
321 and Wordley, 2018). Pescott & Stewart’s concerns about straying from traditional methods of
322 critical appraisal and weighting (e.g., manual risk-of-bias assessments and inverse-variance
323 weightin) may be understandable, but we strongly believe that embracing alternative weighting
324 methods present massive opportunities to advance and future-proof evidence synthesis against
325 the mounting challenges we face in synthesising evidence. We should always strive to maintain
326 high standards of rigour in evidence synthesis, but we must not let the perfect be the enemy of
327 the good when it comes to integrating study quality data into meta-analyses. By embracing
328 alternative weighting methods, we can ultimately increase the efficiency, usefulness, and scale
329 of evidence synthesis through automating critical appraisal, weighting, the regular updating of
330 syntheses.

331

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339

340 **Conflict of Interest**

341 The authors declare no conflicts of interest.

342

343 **Authors contributions**

344 APC led the writing of this manuscript and all other authors contributed critically to drafts, as well
345 as giving final approval for publication.

346

347 **Data Availability Statement**

348 There is no data associated with this article.

349

350 **Supporting Information**

351 There is no Supporting Information associated with this article.

352

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