

This is a repository copy of *Reproducible research practices, openness and transparency in health economic evaluations: study protocol for a cross-sectional comparative analysis*.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/157116/>

Version: Accepted Version

Article:

Catalá-López, F., Caulley, L., Ridao, M. et al. (10 more authors) (2020) Reproducible research practices, openness and transparency in health economic evaluations: study protocol for a cross-sectional comparative analysis. *BMJ Open*. e034463. ISSN 2044-6055

<https://doi.org/10.1136/bmjopen-2019-034463>

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

BMJ Open

Reproducible research practices, openness and transparency in health economic evaluations: study protocol for a cross-sectional comparative analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-034463.R1
Article Type:	Protocol
Date Submitted by the Author:	20-Dec-2019
Complete List of Authors:	Catalá-López, Ferrán; National School of Public Health, Institute of Health Carlos III, Department of Health Planning and Economics Caulley, Lisa; Ottawa Hospital Research Institute Ridao, Manuel; Instituto Aragonés de Ciencias de la Salud (IACS), Red de Investigación en Servicios de Salud en Enfermedades Crónicas (REDISSEC) Hutton, Brian; University of Ottawa, Ottawa, Ontario, Canada, Huseureau, Don; University of Ottawa Drummond, Mike; University of York, Centre for Health Economics Alonso-Arroyo, Adolfo; University of Valencia, Department of History of Science and Documentation; 5Unidad de Información e Investigación Social y Sanitaria-UISYS, University of Valencia and Spanish National Research Council (CSIC) Pardo-Fernández, Manuel; AEMPS Bernal-Delgado, Enrique; Health Sciences Institute in Aragon (IACS) IIS Aragon, Meneu, Ricard; Fundación Instituto de Investigación en Servicios de Salud Tabares, Rafael; University of Valencia Repullo, José; National School of Public Health, Institute of Health Carlos III, Department of Health Planning and Economics Moher, David; Ottawa Hospital Research Institute, Ottawa Methods Centre
Primary Subject Heading:	Health economics
Secondary Subject Heading:	Medical publishing and peer review, Public health, Research methods
Keywords:	Cost-effectiveness analysis, Data sharing, Methodology, Quality, Reporting, Reproducibility

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Note from the Editors: Instructions for reviewers of study protocols

Since launching in 2011, BMJ Open has published study protocols for planned or ongoing research studies. If data collection is complete, we will not consider the manuscript.

Publishing study protocols enables researchers and funding bodies to stay up to date in their fields by providing exposure to research activity that may not otherwise be widely publicised. This can help prevent unnecessary duplication of work and will hopefully enable collaboration. Publishing protocols in full also makes available more information than is currently required by trial registries and increases transparency, making it easier for others (editors, reviewers and readers) to see and understand any deviations from the protocol that occur during the conduct of the study.

The scientific integrity and the credibility of the study data depend substantially on the study design and methodology, which is why the study protocol requires a thorough peer-review.

BMJ Open will consider for publication protocols for any study design, including observational studies and systematic reviews.

Some things to keep in mind when reviewing the study protocol:

- Protocol papers should report planned or ongoing studies. The dates of the study should be included in the manuscript.
- Unfortunately we are unable to customize the reviewer report form for study protocols. As such, some of the items (i.e., those pertaining to results) on the form should be scored as Not Applicable (N/A).
- While some baseline data can be presented, there should be no results or conclusions present in the study protocol.
- For studies that are ongoing, it is generally the case that very few changes can be made to the methodology. As such, requests for revisions are generally clarifications for the rationale or details relating to the methods. If there is a major flaw in the study that would prevent a sound interpretation of the data, we would expect the study protocol to be rejected.

1
2
3
4
5
6
7
8
9
10
11
12
13

1 **Reproducible research practices, openness and transparency in health**
2 **economic evaluations: study protocol for a cross-sectional comparative**
3 **analysis**

4 Ferrán Catalá-López^{1,2,3*}, Lisa Caulley^{3,4,5}, Manuel Ridao⁶, Brian Hutton^{3,7}, Don
5 Husereau^{8,9}, Michael F Drummond¹⁰, Adolfo Alonso-Arroyo^{11,12}, Manuel Pardo-
6 Fernández¹³, Enrique Bernal-Delgado⁶, Ricard Meneu¹⁴, Rafael Tabarés-Seisdedos²,
7 José R. Repullo¹, David Moher^{3,7}

- 8 1. Department of Health Planning and Economics, National School of Public
9 Health, Institute of Health Carlos III, Madrid, Spain
10 2. Department of Medicine, University of Valencia/INCLIVA Health Research
11 Institute and CIBERSAM, Valencia, Spain
12 3. Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa,
13 Ontario, Canada
14 4. Otolaryngology-Head and Neck Surgery Department, Ottawa Hospital, Ottawa,
15 Ontario, Canada
16 5. Department of Epidemiology, Erasmus University Medical Center, Rotterdam,
17 The Netherlands
18 6. Instituto Aragonés de Ciencias de la Salud (IACS), Red de Investigación en
19 Servicios de Salud en Enfermedades Crónicas (REDISSEC), Zaragoza, Spain
20 7. School of Epidemiology and Public Health, University of Ottawa, Ottawa,
21 Ontario, Canada
22 8. Institute of Health Economics, Edmonton, Alberta, Canada
23 9. Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
24 10. Centre for Health Economics, University of York, York, United Kingdom
25 11. Department of History of Science and Documentation, University of Valencia,
26 Valencia, Spain
27 12. Information and Social and Health Research Unit (UISYS), University of Valencia
28 and Spanish National Research Council (CSIC), Valencia, Spain
29 13. Spanish Medicines and Healthcare Products Agency (AEMPS), Madrid, Spain
30 14. Fundación Instituto de Investigación en Servicios de Salud, Valencia, Spain

31 Email addresses: *Contact author

32 *FC-L: ferran_catala@outlook.com

33 LC: lic955@mail.harvard.edu

34 MR: ridao_man@gva.es

35 BH: bhutton@ohri.ca

36 DH: don.husereau@gmail.com

37 MFD: mike.drummond@york.ac.uk

38 AA-A: adolfo.alonso@uv.es

39 MP-F: mapardo@ucm.es

40 EB-D: ebernal.iacs@aragon.es

41 RM: ricard.meneu@gmail.com

42 RT-S: rafael.tabares@uv.es

43 JRR: jrepullo@isciii.es

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

44 DM: dmoher@ohri.ca

For peer review only

1
2
3 45 **Abstract**

4
5 46 **Introduction**

6
7 47 There has been a growing awareness of the need for rigorously and transparent
8 48 reported health research, to ensure the reproducibility of studies by future
9 49 researchers. Health economic evaluations, the comparative analysis of alternative
10 50 interventions in terms of their costs and consequences, have been promoted as an
11 51 important tool to inform decision-making. The objective of this study will be to
12 52 investigate the extent to which articles of economic evaluations of healthcare
13 53 interventions indexed in MEDLINE® incorporate research practices that promote
14 54 transparency, openness and reproducibility.
15
16
17 55

18 56 **Methods and analysis**

19
20 57 This is the study protocol for a cross-sectional comparative analysis. We will evaluate a
21 58 random sample of 600 cost-effectiveness analysis publications, a specific form of
22 59 health economic evaluations, indexed in MEDLINE® during 2012 (n=200), 2019 (n=200)
23 60 and 2022 (n=200). We will include published papers written in English reporting an
24 61 incremental cost-effectiveness ratio in terms of costs per life years gained, quality-
25 62 adjusted life years, and/or disability-adjusted life years. Screening and selection of
26 63 articles will be conducted by at least two researchers. Reproducible research practices,
27 64 openness and transparency in each article will be extracted using a standardized data
28 65 extraction form by multiple researchers, with a 33% random sample (n=200) extracted
29 66 in duplicate. Information on general, methodological and reproducibility items will be
30 67 reported, stratified by year, citation of the Consolidated Health Economic Evaluation
31 68 Reporting Standards (CHEERS) statement and journal. Risk ratios with 95% confidence
32 69 intervals will be calculated to represent changes in reporting between 2012-2019, and
33 70 2019-2022.
34
35
36
37
38

39 71 **Ethics and dissemination**

40
41 72 Due to the nature of the proposed study, no ethical approval will be required. All data
42 73 will be deposited in a cross-disciplinary public repository. It is anticipated the study
43 74 findings could be relevant to a variety of audiences. Study findings will be disseminated
44 75 at scientific conferences and published in peer-reviewed journals.
45
46

47 76 **Study registration**

48
49 77 Open Science Framework (osf.io/gzaxr)

50
51 78 **Keywords**

52
53 79 Cost-effectiveness analysis; Data sharing; Methodology; Quality; Reporting;
54 80 Reproducibility.
55

56
57 81
58
59
60

1
2
3 82 **Strengths and limitations of this study**
4

- 5 83 • To our knowledge, this will be the first attempt to examine the extent to which
6 84 health economic evaluations indexed in MEDLINE® incorporate transparency,
7 85 openness and reproducibility research practices.
- 8
9
10 86 • We will be able to collect data on a broad cross-section of health economic
11 87 evaluations and will not restrict inclusion based on the medical specialty,
12 88 disease condition or healthcare intervention.
- 13
14 89 • Study findings could be used to strengthen Open Science strategies and
15 90 recommendations to increase the value of health economic evaluations.
- 16
17 91 • The study may be limited by the inclusion of articles only catalogued in one
18 92 database and written in English.
- 19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

93 Introduction

94 In recent years, there has been a growing awareness of the need for rigorous and
95 transparent reporting of health research, to ensure that studies can be reproduced [1-
96 7]. The value of health research can be improved by increasing transparency and
97 openness of the processes of research design, conduct, analysis and reporting [8,9].
98 Sharing data and materials from health research studies has multiple positive effects
99 within the research community: it is part of good publication practice, in keeping the
100 principles of Open Science; it allows for the conduct of additional analyses to further
101 explore data and generate new hypotheses; it allows access to unpublished data, and
102 it encourages reproducibility in research [10]. Recognizing the potential impact of open
103 research culture, journals are increasingly supporting the use of reporting guidelines,
104 as well as policies and technologies that help to improve transparency [11-13].
105 Scientists are increasingly encouraged to use reproducible research practices, which
106 allow others to perform direct replication of studies using the same data and analytic
107 methods [14,15]. Furthermore, research funders are changing their grant
108 requirements including open data sharing [16,17].

109
110 Health economic evaluations, which compare alternative interventions or programmes
111 in terms of their costs and consequences [18], can help inform resource allocation
112 decisions. A cost-effectiveness analysis, a specific form of economic evaluation that
113 compares alternative options in terms of their costs and their health outcomes, is a
114 valuable tool in health technology assessment processes. Cost-effectiveness analyses
115 have been promoted as an important research methodology for assessing value for
116 money of healthcare interventions and an important source of information for making
117 clinical and policy decisions [19]. Decisions about the use of new interventions in
118 healthcare are often based on health economic evaluations. Efforts to increase
119 transparent conduct and reporting of health economic evaluations have existed for
120 many years [20-30]. For example, the Consolidated Health Economic Evaluation
121 Reporting Standards (CHEERS) statement [30], first published in March 2013, provides
122 recommendations for authors, peer reviewers and journal editors regarding how to
123 prepare reports of health economic evaluations. The aim of CHEERS is to facilitate
124 complete and transparent reporting of health economic evaluations and help more
125 formal critical appraisal and interpretation. As a potential measure of impact [31],
126 CHEERS has been cited over 1000 times in the Web of Science. However, little
127 attention has been given to reproducibility practices such as sharing of study
128 protocols, data and analytic methods (which allow others to recreate the study
129 findings) as part of health economic evaluation studies [22-25,29].

130
131 Previous research has evaluated the impact of economic evaluation guidelines and the
132 reporting quality of published articles. For example, Jefferson et al. [32] previously
133 investigated whether publication (in August 1996) of the BMJ guidelines on peer
134 review of economics submissions made any difference to editorial and peer review
135 processes, quality of submitted manuscripts, and quality of published manuscripts in
136 two high-impact factor medical journals (The BMJ and The Lancet). In a sample of 105
137 articles on economics submissions, 27 (24.3%) were full health economic evaluations.
138 Although Jefferson et al. [32] were not studying reproducibility, openness and
139 transparency directly, they did undertake an assessment of the impact of a reporting

1
2
3 140 guideline for health economic evaluations. A 'before and after' assessment of
4 141 implementation of the guideline was performed to assess how closely the reporting
5 142 guidelines were followed. The authors found that the publication of the guidelines
6 143 helped the editors improve the efficiency of the editorial process but had no impact on
7 144 the reporting quality of health economic evaluations submitted or published.
8
9 145

10 146 The primary objective of this study will be to examine the extent to which articles of
11 147 health economic evaluations of healthcare interventions indexed in MEDLINE®
12 148 incorporate transparency, openness and reproducibility research practices. Secondary
13 149 objectives will be to explore (1) how the reporting and reproducibility characteristics of
14 150 health economic evaluations change between 2012 and 2022, and (2) whether the
15 151 transparency and reproducibility practices have improved after the publication of the
16 152 CHEERS statement in 2013.
17
18
19

20 153

21 154 **Methods and analysis**

22
23
24 155 This is the study protocol for a cross-sectional, comparative analysis. The present
25 156 protocol has been registered within the Open Science Framework (registration
26 157 identifier: osf.io/gzaxr). It is anticipated the study will be conducted during January
27 158 2020 to December 2023.
28
29

30 159 *Eligibility criteria*

31
32 160 We will evaluate a random sample of 600 cost-effectiveness and cost-utility analyses of
33 161 healthcare interventions, indexed in MEDLINE® during 2012 (n=200), 2019 (n=200) and
34 162 2022 (n=200), which focus on a healthcare intervention in humans and reports an
35 163 incremental cost-effectiveness ratio in terms of costs per life years gained, quality-
36 164 adjusted life years or disability-adjusted life years. In particular, this analysis will focus
37 165 on full health economic evaluations that measures health effects in terms of
38 166 prolongation of life, and/or health-related quality of life. We will select this specific
39 167 form of health economic evaluations because many decision-makers and researchers
40 168 have recommended this framework as the standard reference for cost-effectiveness in
41 169 health and medicine [19]. Publications of health economic evaluations will be limited
42 170 to journal articles written in English with an abstract available.
43
44
45
46

47 171 We will exclude editorials, letters, narrative reviews, systematic reviews, meta-
48 172 analysis, methodological articles, retracted publications, and health economic
49 173 evaluations that do not quantify health impacts in terms of life years gained, quality-
50 174 adjusted life years or disability-adjusted life years.
51
52

53 175 *Searching*

54
55 176 To provide a reliable summary of the literature, we will search MEDLINE® through
56 177 PubMed (National Library of Medicine, Bethesda, Maryland, United States) for
57 178 candidate studies throughout three cross-sectional, comparative time periods. First,
58 179 we will search MEDLINE®-indexed articles in 2019 ("reference year") as it is the year
59
60

1
2
3 180 closest to when the protocol for this study was drafted. In part two, we will search for
4 181 articles indexed in 2012 and 2022, respectively, in order to further assess whether the
5 182 transparency and reproducibility practices improved between 2012 (as it is one year
6 183 before the publication of the CHEERS statement in 2013 [30]), and 2022 (10 years
7 184 after). The literature searches will be conducted by an experienced information
8 185 specialist. Our main literature search will be peer-reviewed by a senior health
9 186 information specialist using the Peer Review of Electronic Search Strategies (PRESS)
10 187 checklist [33]. The draft literature search strategy is based on a MEDLINE® search filter
11 188 for economic evaluations [34], and can be found online in the supplementary appendix
12 189 1.

17 190 *Screening*

19 191 All titles and abstracts will be screened using liberal acceleration (where two reviewers
20 192 need to independently exclude a record while only one reviewer needs to include a
21 193 record). We will retrieve the full-text of any citations meeting our eligibility criteria or
22 194 for which eligibility remains unclear. A form for screening full text articles will be pilot-
23 195 tested on fifty articles. Subsequently, at least 2 reviewers will independently screen all
24 196 full text articles. Any discrepancies in screening full-text articles will be resolved via
25 197 discussion or adjudication by a third reviewer if necessary.

29 198 *Data extraction*

31 199 If more than 600 health economic evaluations are identified in the search, we will
32 200 perform data extraction on a random sample of articles stratified by publication year
33 201 (200 in 2022, 2019 and 2012, respectively). If fewer than 200 articles are identified in a
34 202 given year (e.g. 2012), we will randomly select the sufficient number of studies
35 203 published from the preceding year (e.g. October-December 2011) to match the
36 204 number used in the study sample. We will not perform any sample size calculations
37 205 since our study will evaluate multiple indicators that are considered all equally
38 206 important, and they may vary substantially in the proportion to which they are
39 207 satisfied by the included articles. However, 200 articles per year was assumed to be
40 208 sufficient to capture potential differences.

44 209 Data in each article will be extracted using a standardized data extraction form by
45 210 multiple researchers, with a 33% random sample (n=200) extracted in duplicate. All
46 211 data extractors will independently pilot-test the form on thirty included studies to
47 212 ensure consistency in interpretation of data items. Subsequently, data from each study
48 213 will be independently extracted by one of several reviewers. Any discrepancies in the
49 214 data extracted will be resolved via discussion or adjudication by a third researcher if
50 215 necessary. Full articles and supplementary materials with data and analyses will be
51 216 examined for general and methodological characteristics, statements of publicly
52 217 available full protocols and data sets, conflicts of interest and funding disclosures. In
53 218 particular, we will review the final versions of the articles available online.

58 219 The selection and wording of general, methodological and reproducibility indicators
59 220 will be influenced by recommendations from relevant articles on research

221 transparency and reproducibility [4,5,7,8,29,35-41]. The standardized data extraction
222 form will include the following:

223 *General characteristics:*

- 224 - Name of journal;
- 225 - Journal impact factor (according to the latest Journal Citation Report [JCR] at
226 the time of data extraction);
- 227 - Journal type (fully-open access journal or subscription-based journal including
228 those that may have open access content e.g., hybrid);
- 229 - Year of publication;
- 230 - Name, gender and country of corresponding author;
- 231 - Type of condition addressed by the economic evaluation (ICD-10 category);
- 232 - Type of interventions addressed (pharmacological, nonpharmacological, both)
233 and the intervention to which it was compared (the “comparator” e.g. active
234 alternative, usual care or placebo/do nothing) with adequate descriptions
235 [40,41];
- 236 - Type of economic evaluation (single-study based economic evaluation or
237 model-based economic evaluation);
- 238 - Study perspective (e.g. society, healthcare system/provider) and relate this to
239 the costs being evaluated;
- 240 - Time horizon over which costs and outcomes are being evaluated;
- 241 - Discount rate used for costs and outcomes with rationale (when applicable);
- 242 - Health outcomes used as the measure of benefit (e.g. life years gained, quality-
243 adjusted life years or disability-adjusted life years) and their relevance for the
244 type of analysis performed;
- 245 - Measurement of effectiveness (e.g. for single-study based estimates: a
246 description of the design features of the single effectiveness study, and why the
247 single study was a sufficient source of clinical effectiveness; and for synthesis-
248 based estimates: a description of the methods used for identification of
249 included studies and synthesis of clinical effectiveness data);
- 250 - Estimate of resources and costs (including a description of approaches used to
251 estimate resource use associated with the alternative interventions; and
252 describe methods for valuing each resource item in terms of its unit costs);
- 253 - ~~Discussed~~ Discussion of all analytical methods supporting the evaluation (e.g.
254 methods for dealing with skewed, missing or censored data; extrapolation
255 methods; methods for pooling data; methods for handling population
256 heterogeneity and uncertainty such as subgroup analysis); choice of model and
257 model calibration and validation (when applicable);
- 258 - Results including number of ICERs, sensitivity analyses, subgroup or
259 heterogeneity analyses (e.g. variations between subgroups of patients with
260 different baseline characteristics, or other variability in effects), incremental
261 costs and outcomes for base case analysis ICERs (defined as a qualitative
262 representation of the index ICER e.g. “more costs, more outcomes”, “less costs,
263 more outcomes”, “less costs, comparable outcomes”), the cost-effectiveness

- ratio values (defined as quantitative representation of the base case analysis ICER), incremental costs (the ratio's numerator) and health effects (life years gained, quality-adjusted life years or both – the denominator of the ratio for base case analysis);
- Conclusions including favourable if the intervention clearly claims to be the preferred choice (e.g. cited as “cost-effective”, “reduced costs”, “produced cost savings”, “an affordable option”, “value for money”), unfavourable if the final comments are negative (e.g. the intervention is “unlikely to be cost-effective”, “produced higher costs”, “is economically unattractive” or “exceeded conventional thresholds of willingness to pay”) and neutral or uncertain when the intervention of interest do not surpass the comparator and/or when some uncertainty is expressed in the conclusions.
 - Funding (e.g. no statement, no funding, public, private, other, combination of public/private/other);
 - Conflicts of interests (e.g. no statement, statement no conflicts exist, statement conflicts exist).

Enablers for reproducibility, transparency and openness:

- Citation and/or mention of CHEERS statement (e.g. no citation/mention, citation/mention without reporting checklist, citation/mention with reporting checklist);
- Use of CHEERS appropriately (e.g. when CHEERS was used as a reporting guideline to ensure a clear report of the study's design, conduct and findings), inappropriately (e.g. when CHEERS was used as a methodological tool to design or conduct health economic evaluations or as an assessment tool of methodological quality of publications reporting cost-effectiveness research), or in an unclear or neutral manner (e.g. when use was neither appropriate nor inappropriate) [31,42];
- Open access or free availability in PubMed Central (PMC) based on assignment of an specific ID (PMCID) (yes, no);
- Protocol/registration mentioned (e.g. no protocol, full protocol publicly available, full protocol publicly available and preregistered);
- Health economics analysis plan mentioned (e.g. no analysis plan, indicated that analysis plan was available on request, full access to analysis plan along with research protocol) [39]
- Mention of raw data availability (e.g. no data sharing, indicated that raw data were available on request, full access to raw data for reanalysis);
- Mention of access to analytic methods and algorithms (e.g. “code”, “script”, “model”) used to perform analyses (e.g. no access, indicated that analytic methods were available on request, full access to analytic methods for reanalysis);
- Type of data repository used, if appropriate including use of an open globally-scoped repository (e.g. Open Science Framework, Dryad, Mendeley, Zenodo), a

- 1
2
3 306 journal repository (e.g. supplementary appendix or data paper), or other
4 307 repository (e.g. repository from a specific institution, project, or nation);
5
6 308 - Data made available to recreate the index ICERs (base case);
7 309 - Data made available to recreate all core ICERs (base case and heterogeneity
8 310 analysis);
9
10 311 - Data made available to recreate all ICERs (base case, heterogeneity analysis and
11 312 uncertainty analysis) according to reporting standards [30,38];
12
13 313 - Results have undergone rigorous independent replication and reproducibility
14 314 checks (e.g. whether the study claimed to be a replication effort in the
15 315 abstracts and introductions) [4,5]: statement of novel findings (e.g. the cost-
16 316 effectiveness analysis claims that it presents some novel findings), statement of
17 317 replication (e.g. the cost-effectiveness analysis clearly claims that it is a
18 318 replication effort trying to validate previous knowledge, or it is inferred that the
19 319 cost-effectiveness is a replication trying to validate previous knowledge),
20 320 statement of novel findings and replication (e.g. the cost-effectiveness analysis
21 321 claims to be both novel and to replicate previous findings), no statement on
22 322 novelty or replication (e.g. no statement or an unclear statement about
23 323 whether the cost-effectiveness analysis presents a novel finding or replication).

27 324 *Data analysis*

28
29 325 The analysis will be descriptive, with data summarised as frequency for categorical
30 326 items or median and interquartile range for continuous items. We will characterise the
31 327 indicators for the period 2012-2022. The proportion of general, methodological and
32 328 reproducibility indicators stratified by year will be reported, as well as citation use of
33 329 the CHEERS statement, and journal (e.g. according to whether it is an original CHEERS
34 330 endorsed journal or not). The draft list of original CHEERS endorsed journals can be
35 331 found in the supplementary appendix 2. A priori established Fisher's exact tests and
36 332 risk ratios with 95% confidence intervals will be calculated to represent changes in
37 333 reporting between 2012-2019, and 2019-2022. We will explore whether reproducible
38 334 research practices are associated with the citation of the CHEERS statement. We will
39 335 apply the P value < 0.005 threshold for statistical significance, with P values 0.05 to
40 336 0.005 suggestive [5,43,44].

41
42 337 All analyses will be performed using Stata version 16 or higher (StataCorp LP, College
43 338 Station, Texas, USA).

44 339 *Updates and additional analyses*

45
46 340 We plan to conduct a continual surveillance of the health economic literature, keeping
47 341 evidence as up-to-date as possible. Iterations of the searches and review process will
48 342 be repeated at regular intervals (e.g. 3 year intervals after 2022) to continue to present
49 343 timely and accurate findings. Reanalysis of the proposed reproducibility and
50 344 transparency metrics and indicators may offer insight into progressive improvements
51 345 in design, conduct, and analysis of health economic evaluations over time.

1
2
3 346 Any (new) additional analysis examining potential associations between general
4 347 characteristics from extracted studies (e.g. results including index ICER, or funding
5 348 source) and enablers of reproducibility, transparency and openness (e.g. mention of
6 349 CHEERS statement, open access, protocol registration, or mention of raw data) will be
7 350 prospectively reported in a new specific (sub-study) protocol, following standard
8 351 methods described in this paper.
9
10
11
12 352

13 353 **Patient and public involvement**

14
15 354 No patients and/or public were involved in setting the research question, nor they
16 355 were involved in developing plans for design (or implementation) of this study
17 356 protocol.
18
19
20

21 357 **Ethics and dissemination**

22
23 358 To the best of our knowledge, this cross-sectional analysis will be the first attempt to
24 359 investigate the extent to which articles of cost-effectiveness of healthcare
25 360 interventions incorporate transparent, open and reproducible research practices.
26 361 Without complete and transparent reporting of how a health economic evaluation is
27 362 being designed and conducted, it is difficult for readers and potential knowledge users
28 363 to assess its conduct and validity. Strengthening the reproducibility, openness and
29 364 reporting of methods and results can maximize the impact of health economic
30 365 evaluations by allowing more accurate interpretation and use of their findings. We
31 366 anticipate the study could be relevant to a variety of audiences including journal
32 367 editors, peer reviewers, research authors, health technology assessment agencies,
33 368 guideline developers, research funders, educators and other potential key
34 369 stakeholders. Moreover, the study findings could further be used in discussions to
35 370 strengthen Open Science in order to increase value and reduce waste from incomplete
36 371 or unusable reports of health economic evaluations.
37
38
39
40
41

42 372 Any amendments made to this protocol when conducting the analyses will be outlined
43 373 and reported in the final manuscript. Once completed, findings from this study will be
44 374 published in peer-reviewed journals. All data underlying the findings reported in the
45 375 final manuscript will be deposited in a cross-disciplinary public repository, such as the
46 376 Open Science Framework (<https://osf.io/>). In addition, when new data have become
47 377 available, we will update the analysis and present the updated findings at a public
48 378 repository (and we may also seek publication in a peer-reviewed journal).
49
50
51

52 379

53 380 **Abbreviations:**

54 381 CHEERS: Consolidated Health Economic Evaluation Reporting Standards

55
56 382 ICD-10: International Statistical Classification of Diseases and Related Health Problems,
57 383 10th revision
58
59
60

1
2
3 384 ICER: Incremental Cost Effectiveness Ratio
4
5 385 JCR: Journal Citation Report
6
7 386 PMC: PubMed Central
8
9 387 PMCID: PubMed Central ID
10
11 388 PRESS: Peer Review of Electronic Search Strategies
12

13 389

15 390 **Ethical approval:** This manuscript outlines a protocol for a cross-sectional analysis that
16 391 will undertake secondary data analysis and hence does not require ethical approval.

18 392 **Contributors:** All authors contributed to conceptualizing and designing the study. FC-L
19 393 drafted the manuscript. LC, MR, BH, DH, MFD, AA-A, MP-F, EB-D, RM, RT-S, JRR, and
20 394 DM commented for important intellectual content and made revisions. All authors
21 395 read and approved the final version of the manuscript. FC-L accepts full responsibility
22 396 for the finished manuscript and controlled the decision to publish.

25 397 **Funding:** FC-L and RT-S are supported by the Institute of Health Carlos III/CIBERSAM.
26 398 BH is supported by a New Investigator Award from the Canadian Institutes of Health
27 399 Research and the Drug Safety and Effectiveness Network. MR and EB-D are supported
28 400 by the Institute of Health Carlos III/Spanish Health Services Research on Chronic
29 401 Patients Network (REDISSEC). DM is supported by a University Research Chair,
30 402 University of Ottawa. The funders were not involved in the design of the protocol or
31 403 decision to submit the protocol for publication, nor will they be involved in any aspect
32 404 of the study conduct. The views expressed in this manuscript are those of the authors
33 405 and many not be understood or quoted as being made on behalf of, or reflecting the
34 406 position of, the funder(s) or any institution.

39 407 **Competing interests:** None declared.
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

408 **References**

- 409 1. Nosek BA, Alter G, Banks GC, Borsboom D, Bowman SD, Breckler SJ, et al.
410 Scientific standards. Promoting an open research culture. *Science*.
411 2015;348(6242):1422-5. doi: 10.1126/science.aab2374. PMID: 26113702.
- 412 2. Begley CG, Buchan AM, Dirnagl U. Robust research: Institutions must do their
413 part for reproducibility. *Nature*. 2015;525(7567):25-7. doi: 10.1038/525025a.
414 PMID: 26333454.
- 415 3. Goodman SN, Fanelli D, Ioannidis JP. What does research reproducibility mean?
416 *Sci Transl Med*. 2016;8(341):341ps12. doi: 10.1126/scitranslmed.aaf5027.
417 PMID: 27252173.
- 418 4. Iqbal SA, Wallach JD, Khoury MJ, Schully SD, Ioannidis JP. Reproducible
419 Research Practices and Transparency across the Biomedical Literature. *PLoS*
420 *Biol*. 2016;14(1):e1002333. doi: 10.1371/journal.pbio.1002333. PMID:
421 26726926.
- 422 5. Wallach JD, Boyack KW, Ioannidis JPA. Reproducible research practices,
423 transparency, and open access data in the biomedical literature, 2015-2017.
424 *PLoS Biol*. 2018;16(11):e2006930. doi: 10.1371/journal.pbio.2006930. PMID:
425 30457984.
- 426 6. Naudet F, Sakarovitch C, Janiaud P, Cristea I, Fanelli D, Moher D, Ioannidis JPA.
427 Data sharing and reanalysis of randomized controlled trials in leading
428 biomedical journals with a full data sharing policy: survey of studies published
429 in The BMJ and PLOS Medicine. *BMJ*. 2018;360:k400. doi: 10.1136/bmj.k400.
430 PMID: 29440066.
- 431 7. Page MJ, Altman DG, Shamseer L, McKenzie JE, Ahmadzai N, Wolfe D, Yazdi F,
432 Catalá-López F, Tricco AC, Moher D. Reproducible research practices are
433 underused in systematic reviews of biomedical interventions. *J Clin Epidemiol*.
434 2018;94:8-18. doi: 10.1016/j.jclinepi.2017.10.017. PMID: 29113936.
- 435 8. Ioannidis JP, Greenland S, Hlatky MA, Khoury MJ, Macleod MR, Moher D, Schulz
436 KF, Tibshirani R. Increasing value and reducing waste in research design,
437 conduct, and analysis. *Lancet*. 2014;383(9912):166-75. doi: 10.1016/S0140-
438 6736(13)62227-8. PMID: 24411645.
- 439 9. Chan AW, Song F, Vickers A, Jefferson T, Dickersin K, Gøtzsche PC, Krumholz
440 HM, Ghersi D, van der Worp HB. Increasing value and reducing waste:
441 addressing inaccessible research. *Lancet*. 2014;383(9913):257-66. doi:
442 10.1016/S0140-6736(13)62296-5. PMID: 24411650.
- 443 10. Sharing clinical trial data: maximizing benefits, minimizing risk. Washington, DC:
444 The National Academies Press; 2015.
- 445 11. Moher D. Reporting guidelines: doing better for readers. *BMC Med*.
446 2018;16(1):233. doi: 10.1186/s12916-018-1226-0. PMID: 30545364
- 447 12. Loder E, Groves T. The BMJ requires data sharing on request for all trials *BMJ*.
448 2015;350:h2373. doi: 10.1136/bmj.h2373. PMID: 25953153.
- 449 13. Taichman DB, Backus J, Baethge C, Bauchner H, de Leeuw PW, Drazen JM, et al.
450 Sharing Clinical Trial Data: A Proposal from the International Committee of

- 1
2
3 451 Medical Journal Editors. PLoS Med. 2016;13(1):e1001950. doi:
4 452 10.1371/journal.pmed.1001950. PMID: 26789528.
- 5
6 453 14. Krumholz HM, Waldstreicher J. The Yale Open Data Access (YODA) Project—A
7 454 Mechanism for Data Sharing. N Engl J Med. 2016;375(5):403-5. doi:
8 455 10.1056/NEJMp1607342. PMID: 27518657.
- 9
10 456 15. Bertagnolli MM, Sartor O, Chabner BA, Rothenberg ML, Khozin S, Hugh-Jones C,
11 457 et al. Advantages of a Truly Open-Access Data-Sharing Model. N Engl J Med.
12 458 2017;376(12):1178-1181. doi: 10.1056/NEJMs1702054.
- 13
14 459 16. Collins FS, Tabak LA. Policy: NIH plans to enhance reproducibility. Nature.
15 460 2014;505(7485):612-3. PMID: 24482835.
- 16
17 461 17. Schiltz M. Science Without Publication Paywalls: cOAlition S for the Realisation
18 462 of Full and Immediate Open Access. PLoS Med. 2018;15(9):e1002663. doi:
19 463 10.1371/journal.pmed.1002663. PMID: 30178782.
- 20
21 464 18. Drummond MF, Sculpher MJ, Torrance G, O'Brien J, Stoddart GL. Methods for
22 465 the economic evaluation of health care programmes. 3rd ed. Oxford: Oxford
23 466 University Press; 2005.
- 24
25 467 19. Gold MR, Siegel JE, Russell LB, Weinstein MC. Cost-effectiveness in health and
26 468 medicine. Oxford: Oxford University Press; 1996.
- 27
28 469 20. Hillman AL, Eisenberg JM, Pauly MV, Bloom BS, Glick H, Kinosian B, Schwartz JS.
29 470 Avoiding bias in the conduct and reporting of cost-effectiveness research
30 471 sponsored by pharmaceutical companies. N Engl J Med. 1991;324(19):1362-5.
31 472 PMID: 1901959.
- 32
33 473 21. Bell CM, Urbach DR, Ray JG, Bayoumi A, Rosen AB, Greenberg D, Neumann PJ.
34 474 Bias in published cost effectiveness studies: systematic review. BMJ.
35 475 2006;332(7543):699-703. PMID: 16495332.
- 36
37 476 22. Rennie D, Luft HS. Pharmacoeconomic analyses: making them transparent,
38 477 making them credible. JAMA. 2000;283(16):2158-60. PMID: 10791510.
- 39
40 478 23. Poole C, Agrawal S, Currie CJ. Let cost effectiveness models be open to scrutiny.
41 479 BMJ. 2007;335(7623):735. PMID: 17932167.
- 42
43 480 24. Cohen JT, Neumann PJ, Wong JB. A Call for open-source cost-effectiveness
44 481 analysis. Ann Intern Med. 2017;167(6):432-433. doi: 10.7326/M17-1153. PMID:
45 482 28847014.
- 46
47 483 25. Dunlop WCN, Mason N, Kenworthy J, Akehurst RL. Benefits, challenges and
48 484 potential strategies of open source health economic models.
49 485 Pharmacoeconomics. 2017;35(1):125-128. doi: 10.1007/s40273-016-0479-8.
50 486 PMID: 27928759.
- 51
52 487 26. Neumann PJ, Sanders GD. Cost-Effectiveness Analysis 2.0. N Engl J Med.
53 488 2017;376(3):203-205. doi: 10.1056/NEJMp1612619. PMID: 28099837.
- 54
55 489 27. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of
56 490 economic submissions to the BMJ. The BMJ Economic Evaluation Working
57 491 Party. BMJ. 1996;313(7052):275-83. PMID: 8704542
- 58
59 492 28. Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, et al.
60 493 Recommendations for Conduct, Methodological Practices, and Reporting of
494 494 Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- Medicine. JAMA. 2016;316(10):1093-103. doi: 10.1001/jama.2016.12195. PMID: 27623463.
29. Neumann PJ, Kim DD, Trikalinos TA, Sculpher MJ, Salomon JA, Prosser LA, et al. Future Directions for Cost-effectiveness Analyses in Health and Medicine. *Med Decis Making*. 2018;38(7):767-777. doi:10.1177/0272989X18798833. PMID: 30248277.
30. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al; CHEERS Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *BMJ*. 2013;346:f1049. doi: 10.1136/bmj.f1049. PMID: 23529982.
31. Caulley L, Khoury M, Whelan J, Ferraro J, Catalá-López F, Cheng W, et al. Citation analysis of reporting guidelines [Internet]. OSF; 2019. Available from: osf.io/v46s2
32. Jefferson T, Smith R, Yee Y, Drummond M, Pratt M, Gale R. Evaluating the BMJ guidelines for economic submissions: prospective audit of economic submissions to BMJ and The Lancet. *JAMA*. 1998;280(3):275-7. PMID: 9676680.
33. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol*. 2016;75:40-6. doi: 10.1016/j.jclinepi.2016.01.021. PMID: 27005575.
34. Glanville J, Kaunelis D, Mensinkai S. How well do search filters perform in identifying economic evaluations in MEDLINE and EMBASE. *Int J Technol Assess Health Care*. 2009;25(4):522-9. doi: 10.1017/S0266462309990523. PMID: 19845982.
35. Nosek BA, Ebersole CR, DeHaven AC, Mellor DT. The preregistration revolution. *Proc Natl Acad Sci U S A*. 2018;115(11):2600-2606. doi: 10.1073/pnas.1708274114. PMID: 29531091.
36. Wilkinson MD, Dumontier M, Aalbersberg IJ, Appleton G, Axton M, Baak A, et al. The FAIR Guiding Principles for scientific data management and stewardship. *Sci Data*. 2016;3:160018. doi: 10.1038/sdata.2016.18. PMID: 26978244.
37. Aczel B, Szasz B, Sarafoglou A, Kekecs Z, Kucharský Š, Benjamin D, et al. A consensus-based transparency checklist. *Nat Hum Behav*. 2019 Dec 2. doi: 10.1038/s41562-019-0772-6. [Epub ahead of print] PubMed PMID: 31792401.
38. Chiou CF, Hay JW, Wallace JF, Bloom BS, Neumann PJ, Sullivan SD, et al. Development and validation of a grading system for the quality of cost-effectiveness studies. *Med Care*. 2003;41(1):32-44. PMID: 12544542.
39. Dritisaki M, Gray A, Petrou S, Dutton S, Lamb SE, Thorn JC. Current UK Practices on Health Economics Analysis Plans (HEAPs): Are We Using Heaps of Them? *Pharmacoeconomics*. 2018;36(2):253-257. doi: 10.1007/s40273-017-0598-x. PMID: 29214388.
40. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ*. 2014;348:g1687. doi: 10.1136/bmj.g1687. PMID: 24609605.

- 1
2
3 538 41. Hoffmann TC, Oxman AD, Ioannidis JP, Moher D, Lasserson TJ, Tovey DI, et al.
4 539 Enhancing the usability of systematic reviews by improving the consideration
5 540 and description of interventions. *BMJ*. 2017;358:j2998. doi: 10.1136/bmj.j2998.
6 541 PMID: 28729459.
7
8 542 42. da Costa BR, Cevallos M, Altman DG, Rutjes AW, Egger M. Uses and misuses of
9 543 the STROBE statement: bibliographic study. *BMJ Open*. 2011;1(1):e000048.
10 544 doi: 10.1136/bmjopen-2010-000048. PMID: 22021739.
11
12 545 43. Ioannidis JPA. The Proposal to Lower P Value Thresholds to .005. *JAMA*.
13 546 2018;319(14):1429-1430. doi: 10.1001/jama.2018.1536. PMID: 29566133.
14
15 547 44. Ioannidis JPA. Lowering the P Value Threshold-Reply. *JAMA*. 2018;320(9):937-
16 548 938. doi: 10.1001/jama.2018.8743. PMID: 30193273.
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13

1 **Reproducible research practices, openness and transparency in health**
2 **economic evaluations: study protocol for a cross-sectional comparative**
3 **analysis**

4 Ferrán Catalá-López^{1,2,3*}, Lisa Caulley^{3,4,5}, Manuel Ridao⁶, Brian Hutton^{3,7}, Don
5 Husereau^{8,9}, Michael F Drummond¹⁰, Adolfo Alonso-Arroyo^{11,12}, Manuel Pardo-
6 Fernández¹³, Enrique Bernal-Delgado⁶, Ricard Meneu¹⁴, Rafael Tabarés-Seisdedos²,
7 José R. Repullo¹, David Moher^{3,7}

- 8 1. Department of Health Planning and Economics, National School of Public
9 Health, Institute of Health Carlos III, Madrid, Spain
10 2. Department of Medicine, University of Valencia/INCLIVA Health Research
11 Institute and CIBERSAM, Valencia, Spain
12 3. Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa,
13 Ontario, Canada
14 4. **Ear, Nose and Throat Otolaryngology-Head and Neck Surgery** Department,
15 **Guy's Hospital, London, United Kingdom** **Ottawa Hospital, Ottawa, Ontario,**
16 **Canada**
17 5. Department of **Clinical** Epidemiology, Erasmus University Medical Center,
18 Rotterdam, The Netherlands
19 6. Instituto Aragonés de Ciencias de la Salud (IACS), Red de Investigación en
20 Servicios de Salud en Enfermedades Crónicas (REDISSEC), Zaragoza, Spain
21 7. School of Epidemiology and Public Health, University of Ottawa, Ottawa,
22 Ontario, Canada
23 8. Institute of Health Economics, Edmonton, Alberta, Canada
24 9. Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
25 10. Centre for Health Economics, University of York, York, United Kingdom
26 11. Department of History of Science and Documentation, University of Valencia,
27 Valencia, Spain
28 12. Information and Social and Health Research Unit (UISYS), University of Valencia
29 and Spanish National Research Council (CSIC), Valencia, Spain
30 13. Spanish Medicines and Healthcare Products Agency (AEMPS), Madrid, Spain
31 14. Fundación Instituto de Investigación en Servicios de Salud, Valencia, Spain

32 Email addresses: *Contact author

33 *FC-L: ferran_catala@outlook.com

34 LC: lic955@mail.harvard.edu

35 MR: ridao_man@gva.es

36 BH: bhutton@ohri.ca

37 DH: don.husereau@gmail.com

38 MFD: mike.drummond@york.ac.uk

39 AA-A: adolfo.alonso@uv.es

40 MP-F: mapardo@ucm.es

41 EB-D: ebernal.iacs@aragon.es

42 RM: ricard.meneu@gmail.com

43 RT-S: rafael.tabares@uv.es

1
2
3 44 JRR: jrepullo@isciii.es

4 45 DM: dmoher@ohri.ca

5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

46 **Abstract**

47 **Introduction**

48 There has been a growing awareness of the need for rigorously and transparent
49 reported health research, to ensure the reproducibility of studies by future
50 researchers. Health economic evaluations, the comparative analysis of alternative
51 interventions in terms of their costs and consequences, have been promoted as an
52 important tool to inform decision-making. The objective of this study will be to
53 investigate the extent to which articles of economic evaluations of healthcare
54 interventions indexed in MEDLINE® incorporate **research practices that promote**
55 transparency, openness and reproducibility **research practices**.

57 **Methods and analysis**

58 This is the study protocol for a cross-sectional comparative analysis. We will evaluate a
59 **600** random sample of **600** cost-effectiveness **analysis analyses publications**, a specific
60 form of health economic evaluations, indexed in MEDLINE® during 2012 (n=200), 2019
61 (n=200) and 2022 (n=200). We will include published papers written in English
62 reporting an incremental cost-effectiveness ratio in terms of costs per life years
63 gained, quality-adjusted life years, and/or disability-adjusted life years. Screening and
64 selection of articles will be conducted by at least two researchers. **Potential**
65 **discrepancies will be resolved via discussion**. Reproducible research practices,
66 openness and transparency in each article will be extracted using a standardized data
67 extraction form by multiple researchers, with a 33% random sample (n=200) extracted
68 in duplicate. Information on general, methodological and reproducibility items will be
69 reported, stratified by year, citation of the Consolidated Health Economic Evaluation
70 Reporting Standards (CHEERS) statement and journal. Risk ratios with 95% confidence
71 intervals will be calculated to represent changes in reporting between 2012-2019, and
72 2019-2022.

73 **Ethics and dissemination**

74 Due to the nature of the proposed study, no ethical approval will be required. All data
75 will be deposited in a cross-disciplinary public repository. It is anticipated the study
76 findings could be relevant to a variety of audiences. Study findings will be disseminated
77 at scientific conferences and published in peer-reviewed journals.

78 **Study registration**

79 **Open Science Framework (osf.io/gzaxr)**

80 **Keywords**

81 Cost-effectiveness analysis; Data sharing; Methodology; Quality; Reporting;
82 Reproducibility.

83

1
2
3 84 **Strengths and limitations of this study**
4

- 5 85 • To our knowledge, this will be the first attempt to examine the extent to which
6 86 health economic evaluations indexed in MEDLINE® incorporate transparency,
7 87 openness and reproducibility research practices.
8
9
10 88 • We will be able to collect data on a broad cross-section of health economic
11 89 evaluations and will not restrict inclusion based on the medical specialty,
12 90 disease condition or healthcare intervention.
13
14 91 • Study findings could potentially be used to strengthen Open Science strategies
15 92 and recommendations to increase the value of health economic evaluations.
16
17 93 • A potential limitation could be the study may be limited by the inclusion of
18 94 will include only articles only catalogued in one database and written in English.
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

95 Introduction

96 In recent years, there has been a growing awareness of the need for rigorously and
97 transparently reporting of health research, to ensure that studies can be reproduced
98 [1-7]. The value of health research can be improved by increasing transparency and
99 openness of the processes of research design, conduct, analysis and reporting [8,9].
100 Sharing data and materials from health research studies has multiple positive effects
101 within the research community: with others it is part of good publication practice, is in
102 keeping with the principles of Open Science; and it allows for the conduct of additional
103 analyses to further explore data and generate new hypotheses; it allows access to
104 inclusion of unpublished data, and it encourages reproducibility in research
105 reproducing published findings, and conducting analyses to generate new hypotheses
106 [10]. Recognizing the potential impact of open research culture, journals are
107 increasingly supporting the use of reporting guidelines, as well as policies and
108 technologies that help to improve transparency open research culture [11-13].
109 Scientists are increasingly encouraged to use reproducible research practices, which
110 allow others to perform direct replication of studies redo the same analysis (e.g. direct
111 replication) using the same data and analytic methods [14,15]. Furthermore, research
112 funders are changing their grant requirements including open data sharing [16,17].

114 Health economic evaluations, which compare alternative interventions or programmes
115 in terms of their costs and consequences [18], can help inform resource allocation
116 decisions. A cost-effectiveness analysis, a specific form of economic evaluation
117 involving the comparisons of that compares alternative options in terms of their costs
118 and their health outcomes, is a valuable tool in health technology assessment
119 processes. Cost-effectiveness analysis has been promoted as an important research
120 methodology for assessing value for money of healthcare interventions and an
121 important source of information for making clinical and policy decisions [19]. Decisions
122 about the use of new interventions in healthcare are often based on health economic
123 evaluations. Efforts to increase transparent conduct and reporting of health economic
124 evaluations have existed for many years [20-30]. For example, the Consolidated Health
125 Economic Evaluation Reporting Standards (CHEERS) statement [30], first published in
126 March 2013, provides recommendations for authors, peer reviewers and journal
127 editors regarding how to prepare reports of health economic evaluations. The aim of
128 CHEERS is to facilitate complete and transparent reporting of health economic
129 evaluations and help more formal critical appraisal and interpretation. As a potential
130 measure of impact [31], CHEERS has been cited over 1000 times in the Web of Science.
131 However, little attention has been given to reproducibility practices such as sharing of
132 study protocols, data and analytic methods (which allow others to recreate the study
133 findings) as part of health economic evaluation studies [22-25,29].

135 Previous research has evaluated the impact of economic evaluation guidelines and the
136 reporting quality of published articles. For example, Jefferson et al. [32] previously
137 investigated whether publication (in August 1996) of the BMJ guidelines on peer
138 review of economics submissions made any difference to editorial and peer review
139 processes, quality of submitted manuscripts, and quality of published manuscripts in
140 two high-impact factor medical journals (The BMJ and The Lancet). In a sample of 105
141 articles on economics submissions, 27 (24.3%) were full health economic evaluations.

1
2
3 142 Although Jefferson et al. [32] were not studying reproducibility, openness and
4 143 transparency directly, they did undertake an assessment of the impact of a reporting
5 144 guideline for health economic evaluations. Based on a 'before and after' assessment
6 145 of implementation of the guideline was performed to assess how closely the reporting
7 146 guidelines were followed how closely the reporting guidelines were followed, they.
8 147 The authors found that the publication of the guidelines helped the editors improve
9 148 the efficiency of the editorial process but had no impact on the reporting quality of
10 149 health economic evaluations submitted or published.
11
12
13

14 151 The primary objective of this study will be to examine the extent to which articles of
15 152 health economic evaluations of healthcare interventions indexed in MEDLINE®
16 153 incorporate transparency, openness and reproducibility research practices. Secondary
17 154 objectives will be to explore (1) how the reporting and reproducibility characteristics of
18 155 health economic evaluations change between 2012 and 2022, and (2) whether the
19 156 transparency and reproducibility practices have improved after the publication of the
20 157 CHEERS statement in 2013.
21
22
23

24 158

25 26 159 **Methods and analysis**

27
28 160 This is the study protocol for a cross-sectional, comparative analysis. The present
29 161 protocol has been registered within the Open Science Framework (registration
30 162 identifier: osf.io/gzaxr). It is anticipated the study will be conducted during January
31 163 2020 to December 2023.
32
33

34 164 *Eligibility criteria*

35
36 165 We will evaluate a random sample of 600 cost-effectiveness and cost-utility analyses of
37 166 healthcare interventions, indexed in MEDLINE® during 2012 (n=200), 2019 (n=200) and
38 167 2022 (n=200), which focus on a healthcare intervention in humans and reports an
39 168 incremental cost-effectiveness ratio in terms of costs per life years gained, quality-
40 169 adjusted life years or disability-adjusted life years. In particular, this analysis will focus
41 170 focuses on full health economic evaluations that measures health effects in terms of
42 171 prolongation of life, and/or health-related quality of life. We will select this specific
43 172 form of health economic evaluations because many decision-makers and researchers
44 173 have recommended this framework as the standard reference for cost-effectiveness in
45 174 health and medicine [19]. Publications of health economic evaluations will be limited
46 175 to journal articles written in English with an abstract available.
47
48
49

50
51 176 We will exclude editorials, letters, narrative reviews, systematic reviews, meta-
52 177 analysis, methodological articles, retracted publications, and health economic
53 178 evaluations that do not quantify health impacts in terms of life years gained, quality-
54 179 adjusted life years or disability-adjusted life years.
55
56

57 180 *Searching*

58
59
60

1
2
3 181 To provide a reliable summary of the literature, we will search MEDLINE® through
4 182 PubMed (National Library of Medicine, Bethesda, Maryland, United States) for
5 183 candidate studies throughout three cross-sectional, comparative time periods. First,
6 184 we will search MEDLINE®-indexed articles in 2019 (“reference year”) as it is the year
7 185 closest to when the protocol for this study was drafted. In part two, we will search for
8 186 articles indexed in 2012 and 2022, respectively, in order to further assess whether the
9 187 transparency and reproducibility practices improved between 2012 (as it is one year
10 188 before the publication of the CHEERS statement in 2013 [30]), and 2022 (10 years
11 189 after). The literature searches will be conducted by an experienced information
12 190 specialist. Our main literature search will be peer-reviewed by a senior health
13 191 information specialist using the Peer Review of Electronic Search Strategies (PRESS)
14 192 checklist [33]. The draft literature search strategy is based on a MEDLINE® search filter
15 193 for economic evaluations [34], and can be found online in the supplementary appendix
16 194 1.

195 *Screening*

196 All titles and abstracts will be screened using liberal acceleration (where two reviewers
197 need to independently exclude a record while only one reviewer needs to include a
198 record). We will retrieve the full-text of any citations meeting our eligibility criteria or
199 for which eligibility remains unclear. A form for screening full text articles will be pilot-
200 tested on fifty articles. Subsequently, at least 2 reviewers will independently screen all
201 full text articles. Any discrepancies in screening ~~of titles and abstracts and~~ full-text
202 articles will be resolved via discussion or adjudication by a third reviewer if necessary.

203 *Data extraction*

204 If more than 600 health economic evaluations are identified in the search, we will
205 perform data extraction on a random sample of articles stratified by publication year
206 (200 in 2022, 2019 and 2012, respectively). ~~If fewer than 200 articles are identified in a~~
207 ~~given year (e.g. 2012), we will randomly select the sufficient number of studies~~
208 ~~published from the preceding year (e.g. October-December 2011) to match the~~
209 ~~number used in the study sample.~~ We will not perform any sample size calculations
210 since our study will evaluate multiple indicators that are considered all equally
211 important, and they may vary substantially in the proportion to which they are
212 satisfied ~~already~~ by the included articles. However, 200 articles per year was assumed
213 to be sufficient to capture potential differences.

214 Data in each article will be extracted using a standardized data extraction form by
215 multiple researchers, with a 33% random sample (n=200) extracted in duplicate. All
216 data extractors will independently pilot-test the form on thirty included studies to
217 ensure consistency in interpretation of data items. Subsequently, data from each study
218 will be independently extracted by one of several reviewers. Any discrepancies in the
219 data extracted will be resolved via discussion or adjudication by a third researcher if
220 necessary. Full articles and supplementary materials with data and analyses will be
221 examined for general and methodological characteristics, statements of publicly

222 available full protocols and data sets, conflicts of interest and funding disclosures. In
223 particular, we will review the final versions of the articles available online.

224 The selection and wording of general, methodological and reproducibility indicators
225 will be influenced by recommendations ~~in~~ from relevant articles on research
226 transparency and reproducibility [4,5,7,8,29,35-41]. The standardized data extraction
227 form will include the following:

228 *General characteristics:*

- 229 - Name of journal;
- 230 - Journal impact factor (according to the latest Journal Citation Report [JCR] at
231 the time of data extraction);
- 232 - Journal type (fully-open access journal or subscription-based journal including
233 those that may have open access content e.g., hybrid);
- 234 - Year of publication;
- 235 - Name, gender and country of corresponding author;
- 236 - Type of condition addressed by the economic evaluation (ICD-10 category);
- 237 - Type of interventions addressed (pharmacological, nonpharmacological, both)
238 and the intervention to which it was compared (the “comparator” e.g. active
239 alternative, usual care or placebo/do nothing) with adequate descriptions
240 [40,41];
- 241 - Type of economic evaluation (single-study based economic evaluation or
242 model-based economic evaluation);
- 243 - Study perspective (e.g. society, healthcare system/provider) and relate this to
244 the costs being evaluated;
- 245 - Time horizon over which costs and outcomes are being evaluated;
- 246 - Discount rate used for costs and outcomes with rationale (when applicable);
- 247 - Health outcomes used as the measure of benefit (e.g. life years gained, quality-
248 adjusted life years or disability-adjusted life years) and their relevance for the
249 type of analysis performed;
- 250 - Measurement of effectiveness (e.g. for single-study based estimates: a
251 description of the design features of the single effectiveness study, and why the
252 single study was a sufficient source of clinical effectiveness; and for synthesis-
253 based estimates: a description of the methods used for identification of
254 included studies and synthesis of clinical effectiveness data);
- 255 - Estimate of resources and costs (including a description of approaches used to
256 estimate resource use associated with the alternative interventions; and
257 describe methods for valuing each resource item in terms of its unit costs);
- 258 - ~~Discussed~~ Discussion of all analytical methods supporting the evaluation (e.g.
259 methods for dealing with skewed, missing or censored data; extrapolation
260 methods; methods for pooling data; methods for handling population
261 heterogeneity and uncertainty such as subgroup analysis); choice of model and
262 model calibration and validation (when applicable);

- 1
2
3 263 - Results including number of ICERs, sensitivity analyses, subgroup or
4 264 heterogeneity analyses (e.g. variations between subgroups of patients with
5 265 different baseline characteristics, or other variability in effects), incremental
6 266 costs and outcomes for base case analysis ICERs (defined as a qualitative
7 267 representation of the index ICER e.g. “more costs, more outcomes”, “less costs,
8 268 more outcomes”, “less costs, comparable outcomes”), the cost-effectiveness
9 269 ratio values (defined as quantitative representation of the base case analysis
10 270 ICER), incremental costs (the ratio’s numerator) and health effects (life years
11 271 gained, quality-adjusted life years or both – the ratio’s denominator of the ratio
12 272 for base case analysis);
13 273 - Conclusions including favourable if the intervention clearly claims to be the
14 274 preferred choice (e.g. cited as “cost-effective”, “reduced costs”, “produced cost
15 275 savings”, “an affordable option”, “value for money”), unfavourable if the final
16 276 comments are negative (e.g. the intervention is “unlikely to be cost-effective”,
17 277 “produced higher costs”, “is economically unattractive” or “exceeded
18 278 conventional thresholds of willingness to pay”) and neutral or uncertain when
19 279 the intervention of interest do not surpass the comparator and/or when some
20 280 uncertainty is expressed in the conclusions.
21 281 - Funding (e.g. no statement, no funding, public, private, other, combination of
22 282 public/private/other);
23 283 - Conflicts of interests (e.g. no statement, statement no conflicts exist, statement
24 284 conflicts exist).

25 285 *Enablers for reproducibility, transparency and openness:*

- 26 286 - Citation and/or mention of CHEERS statement (e.g. no citation/mention,
27 287 citation/mention without reporting checklist, citation/mention with reporting
28 288 checklist);
29 289 - Use of CHEERS such as appropriately use (e.g. when CHEERS was used as a
30 290 reporting guideline to ensure a clear report of the study’s design, conduct and
31 291 findings), inappropriately use (e.g. when CHEERS was used as a methodological
32 292 tool to design or conduct health economic evaluations or as an assessment tool
33 293 of methodological quality of publications reporting cost-effectiveness
34 294 research), or in an unclear or neutral manner (e.g. when use was neither
35 295 appropriate nor inappropriate) [31,42];
36 296 - Open access or free availability of free access in PubMed Central (PMC) based
37 297 on assignment of a specific ID (PMCID) (yes, no);
38 298 - Funding (no statement, no funding, public, private, other, combination of
39 299 public/private/other);
40 300 - Conflicts of interests (no statement, statement no conflicts exist, statement
41 301 conflicts exist);
42 302 - Protocol/registration mentioned (e.g. no protocol, full protocol publicly
43 303 available, full protocol publicly available and preregistered);

- 1
2
3 304 - Health economics analysis plan mentioned (e.g. no analysis plan, indicated that
4 305 analysis plan was available on request, full access to analysis plan along with
5 306 research protocol) [39]
6
7 307 - Mention of raw data availability (e.g. no data sharing, indicated that raw data
8 308 were available on request, full access to raw data for reanalysis);
9
10 309 - Mention of access to analytic methods and algorithms (e.g. “code”, “script”,
11 310 “model”) used to perform analyses (e.g. no access, indicated that analytic
12 311 methods were available on request, full access to analytic methods for
13 312 reanalysis);
14
15 313 - Type of data repository used, if appropriate including use of an open globally-
16 314 scoped repository (e.g. Open Science Framework, Dryad, Mendeley, Zenodo), a
17 315 journal repository (e.g. supplementary appendix or data paper), or other
18 316 repository (e.g. repository from a specific institution, project, or nation);
19
20 317 - Data made available reported the data to recreate the index ICERs (base case);
21 318 - Data made available reported the data to recreate all core ICERs (base case and
22 319 heterogeneity analysis);
23
24 320 - Data made available reported the data to recreate all ICERs (base case,
25 321 heterogeneity analysis and uncertainty analysis) according to reporting
26 322 standards [30,38];
27
28 323 - Results have undergone undergoing rigorous independent replication and
29 324 reproducibility checks (e.g. whether the study claimed to be a replication effort
30 325 in the abstracts and introductions) [4,5]: statement of novel findings (e.g. the
31 326 cost-effectiveness analysis claims that it presents some novel findings),
32 327 statement of replication (e.g. the cost-effectiveness analysis clearly claims that
33 328 it is a replication effort trying to validate previous knowledge, or it is inferred
34 329 that the cost-effectiveness is a replication trying to validate previous
35 330 knowledge), statement of novel findings and replication (e.g. the cost-
36 331 effectiveness analysis claims to be both novel and to replicate previous
37 332 findings), no statement on novelty or replication (e.g. no statement or an
38 333 unclear statement about whether the cost-effectiveness analysis presents a
39 334 novel finding or replication).

335 *Data analysis*

336 The analysis will be descriptive, with data summarised as frequency for categorical
337 items or median and interquartile range for continuous items. We will characterise the
338 indicators for the period 2012-2022. The proportion of general, methodological and
339 reproducibility indicators will be reported, stratified by year will be reported, as well as
340 citation use of the CHEERS statement, and journal (e.g. according to whether it is an
341 original CHEERS endorsed journal or not). The draft list of original CHEERS endorsed
342 journals can be found in the supplementary appendix 2. A priori established Fisher’s
343 exact tests and risk ratios with 95% confidence intervals will be calculated to represent
344 changes in reporting between 2012-2019, and 2019-2022. We will explore whether
345 reproducible research practices are associated with the citation of the CHEERS

1
2
3 346 statement. We will apply the P value < 0.005 threshold for statistical significance, with
4 347 P values 0.05 to 0.005 suggestive [5,43,44].

6 348 All analyses will be performed using Stata version 16 15 or higher (StataCorp LP,
8 349 College Station, Texas, USA).

9 350 *Updates and additional analyses*

11 351 We plan to conduct a continual surveillance of the health economic literature, keeping
12 352 evidence as up-to-date as possible. Iterations of the searches and review process will
13 353 be repeated at regular intervals (e.g. 3 year intervals after 2022) to continue to present
14 354 timely and accurate findings. Reanalysis of the proposed reproducibility and
15 355 transparency metrics and indicators may offer insight into progressive improvements
16 356 in design, conduct, and analysis of health economic evaluations over time.

17 357 Any (new) additional analysis examining potential associations between general
18 358 characteristics from extracted studies (e.g. results including index ICER, or funding
19 359 source) and enablers of reproducibility, transparency and openness (e.g. mention of
20 360 CHEERS statement, open access, protocol registration, or mention of raw data) will be
21 361 prospectively reported in a new specific (sub-study) protocol, following standard
22 362 methods described in this paper.

23 363

24 364 **Patient and public involvement**

25 365 No patients and/or public were involved in setting the research question, nor they
26 366 were involved in developing plans for design (or implementation) of this study
27 367 protocol. No patients and/or public will be asked to advice on the interpretation or
28 368 writing up of results. There are no specific plans to disseminate the results of the
29 369 research to the patient community.

30 370 **Ethics and dissemination**

31 371 To the best of our knowledge, this cross-sectional analysis will be the first attempt to
32 372 investigate the extent to which articles of cost-effectiveness of healthcare
33 373 interventions incorporate transparency, openness and reproducibility research
34 374 practices. Without complete and transparent reporting of how a health economic
35 375 evaluation is being designed and conducted, it is difficult for readers and potential
36 376 knowledge users to assess its conduct and validity. Strengthening the reproducibility,
37 377 openness and reporting of methods and results can maximize the impact of health
38 378 economic evaluations by allowing more accurate interpretation and use of their
39 379 findings. We anticipate the study could be relevant to a variety of audiences including
40 380 journal editors, peer reviewers, research authors, health technology assessment
41 381 agencies, guideline developers, research funders, educators and other potential key
42 382 stakeholders. Moreover, the study findings could further be used in discussions to
43 383 strengthen Open Science in order to increase value and reduce waste from incomplete
44 384 or unusable reports of health economic evaluations.

1
2
3 385 Any amendments made to this protocol when conducting the analyses will be outlined
4 386 and reported in the final manuscript. **Once completed**, findings from this study will be
5 387 published in peer-reviewed journals. All data underlying the findings reported in the
6 388 final manuscript will be deposited in a cross-disciplinary public repository, such as the
7 389 Open Science Framework (<https://osf.io/>). **In addition, when new data have become**
8 390 **available, we will update the analysis and present the updated findings at a public**
9 391 **repository (and we may also seek publication in a peer-reviewed journal).**
10
11
12

13 392

14
15 393 **Abbreviations:**16
17 394 CHEERS: Consolidated Health Economic Evaluation Reporting Standards18
19 395 ICD-10: International Statistical Classification of Diseases and Related Health Problems,
20 396 10th revision21
22 397 ICER: Incremental Cost Effectiveness Ratio23
24 398 JCR: Journal Citation Report25
26 399 PMC: PubMed Central27
28 400 PMCID: PubMed Central ID29
30 401 PRESS: Peer Review of Electronic Search Strategies
31
32

33 402

34 403 **Ethical approval:** This manuscript outlines a protocol for a cross-sectional analysis that
35 404 will undertake secondary data analysis and hence does not require ethical approval.36
37 405 **Contributors:** All authors contributed to conceptualizing and designing the study. FC-L
38 406 drafted the manuscript. LC, MR, BH, DH, MFD, AA-A, MP-F, EB-D, RM, RT-S, JRR, and
39 407 DM commented for important intellectual content and made revisions. All authors
40 408 read and approved the final version of the manuscript. FC-L accepts full responsibility
41 409 for the finished manuscript and controlled the decision to publish.42
43
44 410 **Funding:** FC-L and RT-S are supported by the Institute of Health Carlos III/CIBERSAM.
45 411 BH is supported by a New Investigator Award from the Canadian Institutes of Health
46 412 Research and the Drug Safety and Effectiveness Network. MR and EB-D are supported
47 413 by the Institute of Health Carlos III/Spanish Health Services Research on Chronic
48 414 Patients Network (REDISSEC). DM is supported by a University Research Chair,
49 415 University of Ottawa. The funders were not involved in the design of the protocol or
50 416 decision to submit the protocol for publication, nor will they be involved in any aspect
51 417 of the study conduct. The views expressed in this manuscript are those of the authors
52 418 and many not be understood or quoted as being made on behalf of, or reflecting the
53 419 position of, the funder(s) or any institution.54
55 420 **Competing interests:** None declared.
56
57
58
59
60

421 **References**

- 422 1. Nosek BA, Alter G, Banks GC, Borsboom D, Bowman SD, Breckler SJ, et al.
423 Scientific standards. Promoting an open research culture. *Science*.
424 2015;348(6242):1422-5. doi: 10.1126/science.aab2374. PMID: 26113702.
- 425 2. Begley CG, Buchan AM, Dirnagl U. Robust research: Institutions must do their
426 part for reproducibility. *Nature*. 2015;525(7567):25-7. doi: 10.1038/525025a.
427 PMID: 26333454.
- 428 3. Goodman SN, Fanelli D, Ioannidis JP. What does research reproducibility mean?
429 *Sci Transl Med*. 2016;8(341):341ps12. doi: 10.1126/scitranslmed.aaf5027.
430 PMID: 27252173.
- 431 4. Iqbal SA, Wallach JD, Khoury MJ, Schully SD, Ioannidis JP. Reproducible
432 Research Practices and Transparency across the Biomedical Literature. *PLoS*
433 *Biol*. 2016;14(1):e1002333. doi: 10.1371/journal.pbio.1002333. PMID:
434 26726926.
- 435 5. Wallach JD, Boyack KW, Ioannidis JPA. Reproducible research practices,
436 transparency, and open access data in the biomedical literature, 2015-2017.
437 *PLoS Biol*. 2018;16(11):e2006930. doi: 10.1371/journal.pbio.2006930. PMID:
438 30457984.
- 439 6. Naudet F, Sakarovitch C, Janiaud P, Cristea I, Fanelli D, Moher D, Ioannidis JPA.
440 Data sharing and reanalysis of randomized controlled trials in leading
441 biomedical journals with a full data sharing policy: survey of studies published
442 in The BMJ and PLOS Medicine. *BMJ*. 2018;360:k400. doi: 10.1136/bmj.k400.
443 PMID: 29440066.
- 444 7. Page MJ, Altman DG, Shamseer L, McKenzie JE, Ahmadzai N, Wolfe D, Yazdi F,
445 Catalá-López F, Tricco AC, Moher D. Reproducible research practices are
446 underused in systematic reviews of biomedical interventions. *J Clin Epidemiol*.
447 2018;94:8-18. doi: 10.1016/j.jclinepi.2017.10.017. PMID: 29113936.
- 448 8. Ioannidis JP, Greenland S, Hlatky MA, Khoury MJ, Macleod MR, Moher D, Schulz
449 KF, Tibshirani R. Increasing value and reducing waste in research design,
450 conduct, and analysis. *Lancet*. 2014;383(9912):166-75. doi: 10.1016/S0140-
451 6736(13)62227-8. PMID: 24411645.
- 452 9. Chan AW, Song F, Vickers A, Jefferson T, Dickersin K, Gøtzsche PC, Krumholz
453 HM, Gherzi D, van der Worp HB. Increasing value and reducing waste:
454 addressing inaccessible research. *Lancet*. 2014;383(9913):257-66. doi:
455 10.1016/S0140-6736(13)62296-5. PMID: 24411650.
- 456 10. Sharing clinical trial data: maximizing benefits, minimizing risk. Washington, DC:
457 The National Academies Press; 2015.
- 458 11. Moher D. Reporting guidelines: doing better for readers. *BMC Med*.
459 2018;16(1):233. doi: 10.1186/s12916-018-1226-0. PMID: 30545364
- 460 12. Loder E, Groves T. The BMJ requires data sharing on request for all trials *BMJ*.
461 2015;350:h2373. doi: 10.1136/bmj.h2373. PMID: 25953153.
- 462 13. Taichman DB, Backus J, Baethge C, Bauchner H, de Leeuw PW, Drazen JM, et al.
463 Sharing Clinical Trial Data: A Proposal from the International Committee of

- 1
2
3 464 Medical Journal Editors. PLoS Med. 2016;13(1):e1001950. doi:
4 465 10.1371/journal.pmed.1001950. PMID: 26789528.
- 5
6 466 14. Krumholz HM, Waldstreicher J. The Yale Open Data Access (YODA) Project—A
7 467 Mechanism for Data Sharing. N Engl J Med. 2016;375(5):403-5. doi:
8 468 10.1056/NEJMp1607342. PMID: 27518657.
- 9
10 469 15. Bertagnolli MM, Sartor O, Chabner BA, Rothenberg ML, Khozin S, Hugh-Jones C,
11 470 et al. Advantages of a Truly Open-Access Data-Sharing Model. N Engl J Med.
12 471 2017;376(12):1178-1181. doi: 10.1056/NEJMsb1702054.
- 13
14 472 16. Collins FS, Tabak LA. Policy: NIH plans to enhance reproducibility. Nature.
15 473 2014;505(7485):612-3. PMID: 24482835.
- 16
17 474 17. Schiltz M. Science Without Publication Paywalls: cOAlition S for the Realisation
18 475 of Full and Immediate Open Access. PLoS Med. 2018;15(9):e1002663. doi:
19 476 10.1371/journal.pmed.1002663. PMID: 30178782.
- 20
21 477 18. Drummond MF, Sculpher MJ, Torrance G, O'Brien J, Stoddart GL. Methods for
22 478 the economic evaluation of health care programmes. 3rd ed. Oxford: Oxford
23 479 University Press; 2005.
- 24
25 480 19. Gold MR, Siegel JE, Russell LB, Weinstein MC. Cost-effectiveness in health and
26 481 medicine. Oxford: Oxford University Press; 1996.
- 27
28 482 20. Hillman AL, Eisenberg JM, Pauly MV, Bloom BS, Glick H, Kinosian B, Schwartz JS.
29 483 Avoiding bias in the conduct and reporting of cost-effectiveness research
30 484 sponsored by pharmaceutical companies. N Engl J Med. 1991;324(19):1362-5.
31 485 PMID: 1901959.
- 32
33 486 21. Bell CM, Urbach DR, Ray JG, Bayoumi A, Rosen AB, Greenberg D, Neumann PJ.
34 487 Bias in published cost effectiveness studies: systematic review. BMJ.
35 488 2006;332(7543):699-703. PMID: 16495332.
- 36
37 489 22. Rennie D, Luft HS. Pharmacoeconomic analyses: making them transparent,
38 490 making them credible. JAMA. 2000;283(16):2158-60. PMID: 10791510.
- 39
40 491 23. Poole C, Agrawal S, Currie CJ. Let cost effectiveness models be open to scrutiny.
41 492 BMJ. 2007;335(7623):735. PMID: 17932167.
- 42
43 493 24. Cohen JT, Neumann PJ, Wong JB. A Call for open-source cost-effectiveness
44 494 analysis. Ann Intern Med. 2017;167(6):432-433. doi: 10.7326/M17-1153. PMID:
45 495 28847014.
- 46
47 496 25. Dunlop WCN, Mason N, Kenworthy J, Akehurst RL. Benefits, challenges and
48 497 potential strategies of open source health economic models.
49 498 Pharmacoeconomics. 2017;35(1):125-128. doi: 10.1007/s40273-016-0479-8.
50 499 PMID: 27928759.
- 51
52 500 26. Neumann PJ, Sanders GD. Cost-Effectiveness Analysis 2.0. N Engl J Med.
53 501 2017;376(3):203-205. doi: 10.1056/NEJMp1612619. PMID: 28099837.
- 54
55 502 27. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of
56 503 economic submissions to the BMJ. The BMJ Economic Evaluation Working
57 504 Party. BMJ. 1996;313(7052):275-83. PMID: 8704542
- 58
59 505 28. Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, et al.
60 506 Recommendations for Conduct, Methodological Practices, and Reporting of
507 507 Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 508 Medicine. JAMA. 2016;316(10):1093-103. doi: 10.1001/jama.2016.12195.
509 PMID: 27623463.
- 510 29. Neumann PJ, Kim DD, Trikalinos TA, Sculpher MJ, Salomon JA, Prosser LA, et al.
511 Future Directions for Cost-effectiveness Analyses in Health and Medicine. Med
512 Decis Making. 2018;38(7):767-777. doi:10.1177/0272989X18798833. PMID:
513 30248277.
- 514 30. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al;
515 CHEERS Task Force. Consolidated Health Economic Evaluation Reporting
516 Standards (CHEERS) statement. BMJ. 2013;346:f1049. doi: 10.1136/bmj.f1049.
517 PMID: 23529982.
- 518 31. Caulley L, Khoury M, Whelan J, Ferraro J, Catalá-López F, Cheng W, et al.
519 Citation analysis of reporting guidelines [Internet]. OSF; 2019. Available from:
520 osf.io/v46s2
- 521 32. Jefferson T, Smith R, Yee Y, Drummond M, Pratt M, Gale R. Evaluating the BMJ
522 guidelines for economic submissions: prospective audit of economic
523 submissions to BMJ and The Lancet. JAMA. 1998;280(3):275-7. PMID: 9676680.
- 524 33. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS
525 Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin
526 Epidemiol. 2016;75:40-6. doi: 10.1016/j.jclinepi.2016.01.021. PMID: 27005575.
- 527 34. Glanville J, Kaunelis D, Mensinkai S. How well do search filters perform in
528 identifying economic evaluations in MEDLINE and EMBASE. Int J Technol Assess
529 Health Care. 2009;25(4):522-9. doi: 10.1017/S0266462309990523. PMID:
530 19845982.
- 531 35. Nosek BA, Ebersole CR, DeHaven AC, Mellor DT. The preregistration revolution.
532 Proc Natl Acad Sci U S A. 2018;115(11):2600-2606. doi:
533 10.1073/pnas.1708274114. PMID: 29531091.
- 534 36. Wilkinson MD, Dumontier M, Aalbersberg IJ, Appleton G, Axton M, Baak A, et
535 al. The FAIR Guiding Principles for scientific data management and stewardship.
536 Sci Data. 2016;3:160018. doi: 10.1038/sdata.2016.18. PMID: 26978244.
- 537 37. Aczel B, Szaszi B, Sarafoglou A, Kekecs Z, Kucharský Š, Benjamin D, et al. A
538 consensus-based transparency checklist. Nat Hum Behav. 2019 Dec 2. doi:
539 10.1038/s41562-019-0772-6. [Epub ahead of print] PubMed PMID: 31792401.
- 540 38. Chiou CF, Hay JW, Wallace JF, Bloom BS, Neumann PJ, Sullivan SD, et al.
541 Development and validation of a grading system for the quality of cost-
542 effectiveness studies. Med Care. 2003;41(1):32-44. PMID: 12544542.
- 543 39. Dritsaki M, Gray A, Petrou S, Dutton S, Lamb SE, Thorn JC. Current UK Practices
544 on Health Economics Analysis Plans (HEAPs): Are We Using Heaps of Them?
545 Pharmacoeconomics. 2018;36(2):253-257. doi: 10.1007/s40273-017-0598-x.
546 PMID: 29214388.
- 547 40. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better
548 reporting of interventions: template for intervention description and
549 replication (TIDieR) checklist and guide. BMJ. 2014;348:g1687. doi:
550 10.1136/bmj.g1687. PMID: 24609605.

- 1
2
3 551 41. Hoffmann TC, Oxman AD, Ioannidis JP, Moher D, Lasserson TJ, Tovey DI, et al.
4 552 Enhancing the usability of systematic reviews by improving the consideration
5 553 and description of interventions. *BMJ*. 2017;358:j2998. doi: 10.1136/bmj.j2998.
6 554 PMID: 28729459.
7
8 555 42. da Costa BR, Cevallos M, Altman DG, Rutjes AW, Egger M. Uses and misuses of
9 556 the STROBE statement: bibliographic study. *BMJ Open*. 2011;1(1):e000048.
10 557 doi: 10.1136/bmjopen-2010-000048. PMID: 22021739.
11 558 43. Ioannidis JPA. The Proposal to Lower P Value Thresholds to .005. *JAMA*.
12 559 2018;319(14):1429-1430. doi: 10.1001/jama.2018.1536. PMID: 29566133.
13 560 44. Ioannidis JPA. Lowering the P Value Threshold-Reply. *JAMA*. 2018;320(9):937-
14 561 938. doi: 10.1001/jama.2018.8743. PMID: 30193273.
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Supplementary Appendix 1. Draft search for PubMed/MEDLINE®.

1. "cost-benefit analysis"[mh] OR "costs and cost analysis"[mh] OR "cost-effective*" [ti] OR "cost-utility"[ti] OR "economic evaluation"[ti]
2. Journal Article[pt] AND hasabstract[text] AND English[lang] AND ("humans"[mh] OR "humans"[All Fields])
3. Editorial[pt] OR Letter[pt] OR Historical Article[pt] OR Meta-Analysis[pt] OR Retracted Publication[sb] OR Review[pt] OR systematic[sb]
4. #1 AND #2
5. #4 NOT #3

For peer review only

Supplementary Appendix 2. Draft list of original CHEERS endorsed journals.

- Applied Health Economics and Health Policy
- BJOG: An International Journal of Obstetrics and Gynaecology
- BMC Medicine
- The BMJ
- British Journal of Psychiatry
- Clinical Therapeutics
- Cost Effectiveness and Resource Allocation
- The European Journal of Health Economics
- International Journal of Technology Assessment in Health Care
- Journal of Medical Economics
- Pharmacoeconomics
- Value in Health

For more information, see: [https://www.ispor.org/heor-resources/good-practices-for-outcomes-research/article/consolidated-health-economic-evaluation-reporting-standards-\(cheers\)---explanation-and-elaboration](https://www.ispor.org/heor-resources/good-practices-for-outcomes-research/article/consolidated-health-economic-evaluation-reporting-standards-(cheers)---explanation-and-elaboration)

peer review only