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**ISPOR VISION:** ISPOR is the leading global scientific and educational organization for health economics and outcomes research and their use in decision making to improve health.

**ISPOR MISSION:** to promote health economics and outcomes research excellence to improve decision making for health globally.

## 1 **ABSTRACT**

2  
3 As the leading health economics and outcomes research (HEOR) professional society, ISPOR  
4 has a responsibility to establish a uniform, harmonized international code for ethical conduct.  
5 ISPOR has updated its [2008 Code of Ethics](#) to reflect the current research environment. This  
6 code addresses what is acceptable and unacceptable in research, from inception to the  
7 dissemination of its results.

8 There are **nine chapters: 1 – Introduction; 2 – Ethical Principles** (respect, beneficence and  
9 justice) with reference to a non-exhaustive compilation of international, regional, and country-  
10 specific guidelines and standards; **3 – Scope; 4 - Research Design Considerations** (primary  
11 and secondary data related issues, e.g., participant recruitment, population and research  
12 setting, sample size /site selection, incentive/honorarium, administration databases,  
13 registration of retrospective observational studies and modelling studies); **5 – Data**  
14 **Considerations** (privacy and data protection, combining, verification and transparency of  
15 research data, scientific misconduct, etc.); **6 – Sponsorship and Relationships with Others**  
16 (roles of researchers, sponsors, key opinion leaders and advisory board members, research  
17 participants and IRB/EC approval and responsibilities); **7 – Patient Centricity and Patient**  
18 **Engagement** (new addition, with explanation and guidance); **8 - Publication and**  
19 **Dissemination; and 9 - Conclusion and Limitations.**

20 In addition, the ISPOR Code of Ethics Task Force developed a **64-point summary** that is  
21 woven through the first eight chapters. The summary, in its entirety, follows the report (p.23).  
22 **A glossary** follows. Additional material can be found in **10 detailed appendices** that include:  
23 other relevant codes of ethics, HEOR data sources, data protection considerations, recruitment,  
24 safety and reporting, incentive and disclosure requirements, IRB/EC roles and research  
25 participant involvement. These are in a separate attachment and/or can be accessed via this  
26 link to: <https://www.ispor.org/TaskForces/ISPOR-Code-of-Ethics.asp>

27 **PREAMBLE TO CODE OF ETHICS 2017**

28  
29 ISPOR expects its members to adhere to the highest ethical standards because ISPOR's activities and  
30 those of its members affect a number of constituencies. These include, but are not limited to:

- 31 • **Patients** - who are ultimately going to experience the greatest impact of the research.
- 32 • **Health care professionals** - who will be treating or not treating patients with therapies,  
33 medications and procedures made available or not made available due to healthcare research.
- 34 • **Decision-makers and Payers** - who must decide what is covered so as to optimize 1) the health  
35 of patients and 2) resource utilization. This includes:
  - 36 ○ **Government Groups** - who require the results of healthcare research to set policy and  
37 prices.
  - 38 ○ **Insurers** - who base health care coverage and/or payment decisions on healthcare  
39 research.
  - 40 ○ **Employers** - where healthcare research affects their decisions on providing health  
41 benefits.
  - 42 ○ **Administrators and Others**, such as U.S. managed care personnel, - who need results  
43 that are both practical and useful.
- 44 • Professional **Outcomes Researchers**
- 45 • **Pharmaceutical Manufacturers** - whose products are often the subject or focus of healthcare  
46 research.
- 47 • **Colleagues** - where relationships in conducting research and related activities are particularly  
48 critical.
- 49 • **Research employees** – who are concerned about how they are regarded, compensated and  
50 treated by the researchers for whom they work
- 51 • **Students** - where respect and appropriate behavior by researcher / employers is important. They  
52 are the future of the profession.
- 53 • **Clients** - for whom healthcare research is conducted and researcher relationships are  
54 maintained.

55 Through behaviors and practices intended to ensure that healthcare research is designed, conducted,  
56 and reported in the most proper and ethical way possible, the Code is a means for the science of health  
57 economics and outcomes research to avoid or address credibility challenges based on methodology or  
58 bias concerns. By accomplishing this, the various affected constituencies will be able to trust and  
59 benefit from research findings as much as possible. The Code also includes some general ethical  
60 considerations for the Society.

61 As part of membership, members agree to compliance with ISPOR's Code of Ethics when they join or  
62 renew. However, we recognize that members' own organizations may also have ethical codes that  
63 should be followed. We also recognize legal considerations may sometimes be important, for example,  
64 in relation to employment law. ISPOR may deny or revoke membership, participation in groups or  
65 meetings if a member is convicted of a felony or other act or moral turpitude, or upon suspension of a  
66 license in a medical or health profession.

67 **CHAPTER 1: INTRODUCTION**

68  
69 As the leading health economics and outcomes research (HEOR) professional society\*, ISPOR has a  
70 responsibility to establish a uniform, harmonized international set of standards or guidelines for  
71 members to follow. Since 1998, an ISPOR Code of Ethics (Code) has been publicized to HEOR

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\* Pharmacoeconomics is a sub-discipline of health economics. The ISPOR Code of Ethics uses the broader term, health economics, combined with outcomes research to form health economics and outcomes research or HEOR, which has become predominant since ISPOR was founded more than 20 years ago.

72 practitioners. This latest 2107 edition reflects the changing environment in which ISPOR and its  
73 membership conduct research.

74  
75 Those practicing in the HEOR area have a long history of civil discourse and of developing “good  
76 practices” associated with different research designs. Such discussions and the templates developed  
77 are ways to reduce the unwarranted variation in professional outputs. Nonetheless, a code of ethics  
78 differs from a recommended good or best practice recommendation. It is concerned with principles,  
79 such as informed consent, data privacy and equity in healthcare.

80 The core principles embodied in a code of ethics represent values that, on one hand, must not be  
81 compromised but, on the other hand, may need to be weighed against one another. They are the  
82 guiding standards that are essential for the professionalism of researchers, and the confidence that  
83 users and members of other professions can have in HEOR.

84  
85 The composition of ISPOR as an organization is an important preface to what is to follow. The global  
86 nature of ISPOR sets it apart from many other organizations, with differences in cultures and  
87 sometimes, points of view on important issues, such as data privacy. ISPOR members represent  
88 multiple disciplines that approach intellectual problems in HEOR with a variety of tools and research  
89 designs. They differ in the relationships that they have with different healthcare systems around the  
90 globe. They come from diverse employment settings with complex and dynamic structures.

91 As a multidisciplinary, global organization, ISPOR strives for representativeness, transparency, and  
92 balance in its activities, thereby, avoiding the appearance of bias or conflict of interest. This includes,  
93 but is not limited to, sponsorship of its conferences and other activities, as well as presenters at its  
94 conferences. To the extent that it is feasible, ISPOR program planning and selection committees should  
95 have a membership representative from all of its major constituencies. ISPOR should also have a Board  
96 of Directors that is representative of the various constituencies the Society serves.

97 Furthermore, because significant research funding will come from funders with interests in specific  
98 findings (at times commercial, private non-profit, as well as governmental institutions, all have hoped-for  
99 outcomes), ISPOR should continue to maintain its own statement of objectivity and autonomy. ISPOR  
100 strives to assure that its journal, Value in Health, only publishes papers that have gone through a  
101 rigorous peer-review process, and whose authors are listed pursuant to strict criteria.

102  
103 Even though economics is a major part of ISPOR’s identity, price and coverage discussions, and similar  
104 topics, should not be construed as encompassing ISPOR’s total identity. Rather, ISPOR is conscious  
105 of broader ethical issues impacting global and regional medical resource allocation, public health  
106 policies and the global healthcare environment, and, on the research side, topics such as patient  
107 autonomy, patient outcomes and research conduct. These issues include, but are not limited to:  
108 prejudice, equity in healthcare delivery, and access.

109  
110 The HEOR profession and research landscape have changed dramatically since the publication of the  
111 current Code in 2008<sup>1</sup> (Appendix 1) with the increased collection and use of real world data, rise of  
112 health information technology (IT), genomic information, focus on patient centricity, social media, and  
113 privacy issues, among others. Furthermore, most professional codes that ISPOR referenced in the past  
114 have been updated since last publication. Finally, due to the Society’s immense growth in both  
115 membership and geographic coverage, it is important to recognize that there may be conflicting  
116 standards of professional conduct in regions of the world that now need to be considered in ISPOR’s  
117 Code (version 4).

118  
119  
120  
121  
122

Rather than merely reducing unwarranted variance, a code of ethics is intended to promulgate the standards that define what is acceptable and unacceptable in the conduct of all aspects of research, from its inception to the dissemination of its results. This revised Code represents a collective effort to articulate those standards.

123 *Therefore:*

124 - *ISPOR should publicize this Code of Ethics to members and non-members involved in*  
125 *pharmacoeconomics and outcomes research.*

126 - *ISPOR should strive for a balance in sponsorship of its conferences and other activities by providing*  
127 *criteria for accepting of funding and ensuring full transparency, thereby avoiding the appearance of bias*  
128 *or conflict of interest.*

129 - *Because, as a practical matter, most funding will come from different entities, ISPOR should continue*  
130 *to maintain its own statement of objectivity and autonomy.*

131 - *ISPOR should strive to assure that its journal, Value in Health, only publishes papers that have gone*  
132 *through a rigorous peer-review process.*

133 - *ISPOR should have a Board of Directors that is representative of the various constituencies the*  
134 *Society serves.*

135 - *The ISPOR program planning and selection committees should have membership representative of all*  
136 *of its major constituencies.*

137 - *Like other professional societies, ISPOR should be conscious of broader ethical issues impacting*  
138 *global and regional medical resource allocation, public health policies and the global healthcare*  
139 *environment, and research topics such as patient autonomy and research conduct. These issues*  
140 *include, but are not limited to: prejudice, equity in healthcare delivery, and access.*

## 141 **CHAPTER 2: APPLICATION OF ETHICAL PRINCIPLES TO THE ISPOR CODE**

142

143 Both the past and the current Code of Ethics draw from international standards and guidelines. A non-  
144 exhaustive compilation of international, regional, and country-specific guidelines and standards in the  
145 research field including patient engagement resources and publication ethics codes was reviewed and  
146 summarized (Appendix 2). This range of standards includes, but is not limited to, the Belmont Report,  
147 the International Conference on Harmonization Good Clinical Practice (ICH GCP), the Agency for  
148 Healthcare Research and Quality (AHRQ) of the United States, the European Federation of  
149 Pharmaceutical Industries and Associations (EFPIA), Guidelines for Research Ethics in Japan, and the  
150 Genetic Alliance for patient engagement.

151

152 *Therefore:*

153

154 - *Members should maintain a current knowledge of research practices, with due consideration of those*  
155 *practices most relevant to the research that is being done in their own countries.*

156

157 The ISPOR Code closely follows the Belmont Report's three fundamental ethical principles that form the  
158 basis for the National Commission's topic-specific reports and the regulations that incorporate its  
159 recommendations. Application of these principles requires careful consideration of informed and

160 voluntary consent, risks and benefits, and the selection of participants for research.

161  
162 **Respect for persons:** protecting the autonomy of all people; treating them with courtesy and  
163 respect; and allowing for informed and voluntary consent. Researchers must be truthful and  
164 conduct no deception;

165  
166 **Beneficence:** the philosophy of "Do no harm" while maximizing benefits for the research project  
167 and minimizing risks to the research participants; and

168  
169 **Justice:** ensuring reasonable, non-exploitative, and well-considered procedures are  
170 administered fairly — the fair distribution of costs and benefits to potential research participants  
171 — and equally.

172  
173 ISPOR's Code places additional emphasis on privacy, transparency and civility. This reflects the  
174 responsibilities associated with increased data access, the global nature of research, and a broad range  
175 of research participants and health care system stakeholders.

176  
177 *Therefore:*

178  
179 - *Privacy: Members who work in HEOR can be privy to data sources containing protected health*  
180 *information (PHI) and other personal data from patients. It is essential that these data are handled with*  
181 *utmost care so that patient confidentiality be maintained at all times and no breaches to patient privacy*  
182 *occur.*

183 - *Transparency and Integrity: Members must disclose research methods in sufficient detail to permit*  
184 *replication. The funding sources should be clearly acknowledged, and any conflicts of interests declared.*  
185 *Designing, conducting and especially reporting of the study should be an unbiased reflection of the full*  
186 *range of findings generated.*

187 - *Civility: Members' research and discussion should respect the dignity of all participants. Respecting the*  
188 *dignity of patients and providers of care is clearly a responsibility. It is also a responsibility to treat fellow*  
189 *researchers with respect.*

190 All HEOR studies should respect and protect the human subjects enrolled in those studies, using the  
191 principles of the Declaration of Helsinki (1964-2013).<sup>2</sup> Medical research is subject to ethical standards  
192 that promote and ensure respect for all human subjects and protect their health and rights. While the  
193 primary purpose of medical research is to generate new knowledge, this goal can never take  
194 precedence over the rights and interests of individual research participants.

### 195 **CHAPTER 3: SCOPE OF THE CODE**

196  
197 The ISPOR Code of Ethics is specifically oriented to HEOR. While there is overlap with other fields, our  
198 goal is a discipline-oriented Code. It is important to note that the scope of this Code of Ethics does not  
199 include ethical considerations related to the use or impact of specific HEOR measures, e.g., potential  
200 age-related biases implicit in quality-adjusted life years.

201  
202 ISPOR's Code of Ethics covers the conduct of HEOR, but not societal decision making based on HEOR  
203 evidence, such as formation of HTA policies. As long as reporting of research is complete and

204 transparent, users of ISPOR members' research can judge use or impact issues independently. For  
205 more on these issues, please refer to the Second Panel on Cost Effectiveness in Health and Medicine.<sup>3</sup>  
206

207 **Health economics** is a branch of economics, a discipline that analyzes the economic aspects of all  
208 activities designed to improve or maintain health and health care, typically focusing on the costs (inputs)  
209 and the consequences (outcomes) of health care interventions. It is concerned with issues related to  
210 efficiency, effectiveness, utility, value, quality, ethics and behavior in the production and consumption of  
211 health and health care. In broad terms, health economists study the functionality of health care systems  
212 and health-affecting behaviors.<sup>4</sup>  
213

214 **Outcomes research** is the scientific discipline that evaluates the effect of health care interventions on  
215 patient well-being, including clinical, economic and patient-centered outcomes. (ISPOR Book of Terms)  
216

#### 217 **Difference and relationship to other research fields**

218 HEOR is closely related to other common research types, such as clinical trial/studies, non-  
219 interventional observations, epidemiologic investigations, real world research and market research  
220 studies (See Appendix 3 for more information).  
221

222 There is no single legal instrument or practical guidance for HEOR. At times, this results in differences  
223 in definitions and terms across groups and countries. HEOR can utilize any techniques from the  
224 research types mentioned above. The objective is to evaluate the effect of health care interventions on  
225 patient well-being, including clinical, economic, and patient-centered, and other relevant outcomes, as  
226 well as the functioning of health care systems and health-affecting behaviors.  
227

228 *Therefore:*

229  
230 *- Members should adhere to the standards of practice for their respective fields of research and identify*  
231 *any official guidelines and standards used.*  
232

233 This 2017 Code of Ethics covers the following five topics in depth: research design, data  
234 considerations, sponsorship, patient engagement, and publication and dissemination with appendices  
235 providing ancillary detail to these sections.

## 236 **CHAPTER 4: RESEARCH DESIGN CONSIDERATIONS**

237  
238 HEOR comprises a range of research designs from modeling and retrospective analyses using  
239 secondary data to prospective observational and clinical trial designs (See Appendix 4 for more on  
240 HEOR data sources). No matter the chosen research design, HEOR is conducted following the core  
241 scientific principles of objectivity, transparency, reporting, and quality assurance. It is defined by the  
242 objective(s) and the approach, not by the title of the work or the role of those commissioning the work.  
243

### 244 **Primary Data-Related Research Considerations**

#### 245 **Participant Recruitment**

246 ISPOR recognizes that study participants can be recruited via a number of methods.  
247

248  
249 *Therefore,*  
250

251 *From the point of “first contact” researchers should provide potential subjects information about study*  
252 *intentions and how the research is funded, as well as all information mandated in their proposals as*  
253 *reviewed by institutional review boards (IRBs)/research ethics committees (RECs). (See Appendix 5 for*  
254 *more details.)*

255

### 256 **Population and Research Setting**

257 Researchers should be specific with regard to population and setting.

258

259 *Therefore,*

260

261 *Members should describe the analytic study population in terms of persons, geography, time period, and*  
262 *selection criteria. Members should choose, and obtain permissions to use, a suitable research setting*  
263 *and/or existing data or literature to provide information about a specific population to which the study*  
264 *results are meant to apply.*

265

### 266 **Sample Size, Site Selection**

267 Study sample size should not be larger than statistically necessary. Inadequate sample size (too low)  
268 may provide insufficient data to answer the intended research questions or will provide low precision<sup>5</sup>.

269

270 *Therefore,*

271

272 *The number of patients and sites selected for a study should be appropriate to meet the research*  
273 *objectives.*

274

### 275 **Safety / (Serious) Adverse Events**

276 Safety and adverse event reporting (AER) is an important aspect of all primary research involving  
277 patients and medical interventions. The Guideline on good pharmacovigilance practices (GVP)<sup>6</sup> laid  
278 down in the European Union’s Directive 2010/84/EU<sup>7</sup> applies to investigational medicinal products and  
279 non-investigational medicinal products. Similar regulations exist in most other jurisdictions. AER is  
280 applicable to some HEOR activities, including clinical trials, primary research, non-interventional  
281 studies, market research, and real world research. (For more information, see Appendix 6.)

282

283 Researchers are expected to collect and report adverse events, not only due to regulatory and legal  
284 requirements, but also with an understanding of the responsibility to patients and society to  
285 comprehensively inform the safety of treatment options.

286

287 A strong international collaborative approach to post-approval surveillance and mandatory adverse  
288 reporting is critical. Data collected through social and digital media can be useful, but often do not follow  
289 clear pharmacovigilance reporting guidelines because there is no single marketing authorization holder.

290

291 *Therefore:*

292

293 *- The balance of risk or harm to benefit for patients must be considered in HEOR studies, and must be*  
294 *communicated to patients via informed consent.*

295

296 *-Safety and adverse event reporting (AER) are important aspects of all primary research involving*  
297 *patients and medical interventions, are applicable to many HEOR activities, and must follow*  
298 *international guidelines.*

298

299 **Incentive/Honorarium**

300 An 'incentive' or honorarium is any benefit given to a participant to encourage participation in a  
301 research study. It is commonly used in prospective research and surveys to provide participants with  
302 compensation for expenses that may be incurred as part of participating in research. Remuneration is  
303 compensation to investigators or consultants for their work or contribution to the study. For specific  
304 details on incentives and honoraria, see Appendix 7.

305  
306 *Therefore,*

307  
308 *Any such proposed payments are, of course, subject to receivers and providers' internal compliance*  
309 *guideline and IRB/EC approval, and must be detailed in the research proposal submitted for review.*

310  
311 *Researchers need to be diligent in ensuring that the incentive would not induce research participants to*  
312 *accept risks they would not be willing to accept if they were offered a smaller or no incentive.*

313  
314  
315 **Secondary Data-Related Research Considerations:**

316  
317 **Administrative Databases and Other Large Datasets**

318 Health care systems generate operational and administrative data that have been used extensively in  
319 HEOR studies. HEOR uses a wide range of secondary research sources, including proprietary  
320 databases, claims databases, patient registries, routine data sources, systematic reviews, evidence  
321 synthesis, social media, Internet of Things (IoT), and other related sources. Data can range from a  
322 longitudinal administrative database to a constant flow from IoT and wearable devices, or from  
323 controlled clinical trials to unstructured social media feeds.

324  
325 Examples include governmental databases like the US's Center for Medicare and Medicaid Services  
326 (CMS), Chronic Condition Data Warehouse (CCW), SEER Medicare<sup>8</sup>, the United Kingdom's HES<sup>9</sup>,  
327 France's SNIIRAM<sup>10</sup> etc., as well as a number of private databases. Some research involves  
328 combining various datasets (e.g. Medicare Current Beneficiary Survey and Medicare Claims Parts A, B,  
329 C or D). This diversity in types of datasets presents multiple analytic challenges.

330  
331 Because the data were initially collected for another purpose, the key first step for those creating and  
332 then using secondary data is to be sure that all intellectual property rights have been respected and that  
333 the appropriate permissions have been secured. This is typically done by the database supplier. These  
334 permissions include protection of the privacy of the individuals whose characteristics are captured in the  
335 database, as well as their informed consent for secondary use of their data, where applicable. Privacy is  
336 discussed below.

337  
338 The cost of creating databases for secondary use is sometimes borne by governments and the users are  
339 charged nominal fees. When private entities build databases for secondary use they will often do so in  
340 anticipation of higher user fees that make database creation and distribution a worthwhile commercial  
341 endeavor. In either case, the researcher needs to be assured that the database was legally and  
342 ethically constructed.

343  
344 The vast majority of HEOR studies currently conducted involve the analysis of secondary data.  
345 Retrospective observational studies are often conducted using administrative databases or clinical  
346 registries. Modeling studies involve the synthesis and analysis of data from several sources, including  
347 previously conducted clinical trials, clinical registries, routinely available cost data, and the published

348 literature. The use of secondary data has ethical challenges related to the collection and storage of  
349 personal data that are different from those in primary research studies (discussed above), since the data  
350 are already anonymized. If there is doubt or moral concern regarding how the secondary data were  
351 generated, researchers can consider a due diligence process on the data source before using it, or can  
352 use an alternative dataset for the study.

353  
354 There are instances where a secondary database may not be considered de-identified. One example is  
355 the CMS Chronic Condition Warehouse where age and postal zip code information are included.  
356 However, given the large degree of analyst discretion, secondary research studies do raise a number of  
357 ethical challenges relating to the avoidance of methodological bias due to the selective use of the  
358 available data and the inappropriate use of assumptions regarding such things as missing data, the  
359 nature of selection bias, outliers, and so on. Therefore, the most important general ethical principles in  
360 the analysis of secondary data are those of 'transparency and reasonableness, i.e., in the absence of  
361 consensus on principles, a fair process allows us to agree on what is legitimate and fair.'<sup>11</sup>

362  
363 Therefore,

- 364  
365 - *When using secondary data sources initially collected for another purpose, HEOR researchers*  
366 *should ensure that intellectual property rights are respected and that all the appropriate*  
367 *permissions have been secured.*
- 368  
369 - *Given the potential for bias in the analysis of secondary data, the most important general ethical*  
370 *principles are those of 'reasonableness' and 'transparency'.*

### 371 372 373 **Registration of Retrospective Observational Studies**

374 For purposes of this Code, observational studies are defined as analysis of existing datasets.<sup>1213</sup> While  
375 the registration of research is more common for clinical trials than for observational studies, Williams et  
376 al (2010) argue that 'Much of the rationale for the prospective registration of clinical trials applies to the  
377 registration of observational studies'.<sup>14</sup> These obligations include oversight by ethical review boards,  
378 informed consent, and public release of the study findings to advance biomedical knowledge. As with  
379 clinical trials, incomplete reporting of observational studies has been documented. Some researchers  
380 suggest that observational studies are also at increased risk for publication bias or other types of bias,  
381 including misrepresentation of pre-specified analyses or disease classification coding. Such biases are a  
382 concern because they undermine the validity of observational studies, which are an important  
383 component of the medical evidence base in areas of public health, such as detection of rare adverse  
384 events.

385  
386 Therefore,

387  
388 - *In those instances in which study methods include analysis of a database, members should describe*  
389 *approaches, methods, technologies used to ensure data completeness and validity as well as the*  
390 *software package(s) used for data analysis. Members should have the education, training and*  
391 *experience to perform the assigned tasks.*

392  
393 - *While registration of observational studies is generally not required at this time, members are*  
394 *encouraged to register such studies prospectively to recognize ethical obligations to patients and to*  
395 *avoid the potential for publication bias.*

396  
397 - Where a HEOR study is being conducted alongside a clinical study gathering data prospectively (such  
398 as a clinical trial or observational study), where possible members should ensure that the clinical study  
399 concerned has been registered on ClinicalTrials.gov, Patient Registries (e.g. patientregistry.ahrq.gov),  
400 EU electronic Register of Post-Authorisation Studies (EU PAS Register)<sup>15</sup>, or equivalent database in  
401 their own country.

402  
403 ISPOR has published a number of Good Practices for Outcomes Research Reports<sup>16</sup> on conducting  
404 outcomes research (clinical, economic or patient-reported) or using outcomes research in health care  
405 decisions. While these reports do not address ethical principles directly, the specification of good  
406 research methods is an important component of recognizing and eliminating analytic bias.

### 407 **Modeling Studies**

408  
409 In these HEOR studies, secondary data from multiple sources are synthesized using a decision-analytic  
410 model. Although this is the main application of modeling, models are sometimes used to extrapolate  
411 costs and benefits beyond the end of a clinical trial in a primary research study. The ethical principles  
412 discussed here apply equally to both situations.

413  
414 The general ethical principles of reasonableness and transparency suggest a number of approaches for  
415 the conduct of modeling studies. ISPOR with the Society for Medical Decision Making published seven  
416 Modeling Good Research Practices Task Force Reports<sup>17</sup>. The seventh, on model transparency and  
417 validation<sup>18</sup>, is the most relevant task force report to the ISPOR Code of Ethics.

418  
419 *Therefore,*

420  
421 *In conducting modeling studies, members should ensure that the input parameters are estimated based*  
422 *on a comprehensive review of the available literature. For the key parameters of the model (e.g., the*  
423 *estimate of relative treatment effect) it may be necessary to conduct a full systematic review and meta-*  
424 *analysis.*

425  
426 However, decision-analytic models typically rely on numerous parameter estimates and it will not be  
427 possible to undertake a full systematic review for each. Therefore, members should be transparent about  
428 the estimates they use for key parameters, provide the logic they used in selecting particular estimates  
429 and explore the impact of their choices through sensitivity analysis. (Sensitivity analysis is widely used in  
430 economic evaluation and explores the sensitivity of the study results to the variation in the input  
431 parameters.)

432  
433 Another important feature of modeling studies is the need to make assumptions, either about the  
434 parameter estimates in situations where data are absent or inadequate parameter uncertainty<sup>19</sup>, or about  
435 model structure (structural uncertainty). The ethical principles of reasonableness and transparency  
436 would dictate that any assumptions are clearly explained and justified. In addition, sensitivity analyses  
437 should be conducted to explore the importance (in terms of the overall estimate of cost-effectiveness) of  
438 the assumptions made.

439  
440 Reporting is discussed further in Chapter 8: Publication and Dissemination.

## CHAPTER 5: DATA CONSIDERATIONS

This section provides guidance on data considerations in privacy, data protection, combining research data, data validity<sup>20</sup>, transparency, and scientific misconduct. Members should ensure selection of suitable data sources and adequate sample size to power the question(s) being studied.

### Privacy and Data Protection

Protecting participants' privacy is paramount to all forms of clinical research, including HEOR. Regulations such as the EU GDPR<sup>21</sup> U.S. HIPAA<sup>22</sup>), Japan APPI<sup>23</sup> cover the collection of data relating to an identifiable person. For data protection purposes, original holders of personal data can, if contractually bound, transfer personal data to other parties without seeking additional explicit permission of the data subject, as long as the data are being used for a purpose for which the original holder has a lawful basis to process the personal data, including the consent of the data subject. This would need to be an integral part of the informed consent process and would require IRB approval. Details of data processing, security, storing, transfer, and participants' rights to their personal data are detailed in Appendix 8.

### Combining Research Data

It is sometimes possible to enrich an existing database by linking additional information that is relevant to the individual patient or the provider. Examples include linking socioeconomic information about the neighborhood surrounding the patient's home or the training history of the specific provider delivering a service. The most effective linkages take full advantage of the identifying characteristics of the patient or the provider. Adding data to an existing database can lead to the subtle erosion of privacy protections. As a result, some database providers insist on limiting potential links. It is critical to protect the commitment to privacy during and after the linkage of additional data. Combining of research data must also have been approved by the IRB.

### Data Verification

On occasion, access to these data may be requested by journal reviewers or other researchers wishing to verify the analyses used in the research. It is important that researchers, sponsors and the owners of data recognize that the credibility of the research is lessened if other parties cannot adequately verify it.

This is particularly important if one of the objectives of the research is to inform health care decision makers, who in turn may have to justify the basis on which they made a particular decision. This suggests that the maximum level of access, within the law, should be granted by researchers to anonymized, group-level data and that the contracts for undertaking the research should reflect this consideration.

*Therefore:*

*- When a database (from primary data collection and/or secondary data use) is analyzed, members should provide a description of approaches, tools, and technologies used to store the data and maintain patient privacy/confidentiality and de-identification.*

*- Personal data should be maintained securely and adequate back-up should be maintained. Data access should be limited to authorized individuals. Control systems should be put in place to ensure authenticity, integrity, and confidentiality of data records when transmitted electronically.*

*- Researchers should offer the maximum level of access to the anonymized, group-level data used in*

491 *their research. If data access is restricted by proprietary or contractual considerations, those*  
492 *considerations should be disclosed. If journal reviewers deem it important that statistical review of*  
493 *proprietary data be conducted, authors should work with both the data owners and the reviewers to find*  
494 *appropriate confidential arrangements for such review whenever feasible.*

## 496 **Transparency of Research and Data**

497  
498 Transparency and replicability are crucial to HEOR. Transparency of data and replicability of results are  
499 important issues that pose challenges for authors, reviewers and journals (Cochrane 2015)<sup>24</sup>. Some  
500 journals have explicit data policies; ISPOR's journal *Value in Health* has its own, and ISPOR members  
501 – as well as all contributors – are expected to comply with this policy<sup>25</sup>.

502  
503 Nevertheless, it is recognized that for many, if not most reviewers, detailed review of data, programs,  
504 and results is not feasible in the context of performing a timely manuscript review. For those who are  
505 able to do so, such review is encouraged (see Cochrane 2015). Those who are not able to do so, but  
506 have reason to believe that data review is indicated, should inquire with the editor about the possibility  
507 of employing an independent statistical reviewer.

508  
509 *Therefore:*

510  
511 *- Members' hypotheses and research designs should be defined a priori, reported transparently,*  
512 *defended relative to alternatives, and planned to recognize and minimize all types of bias.*

513  
514 *- Members should fully disclose the identity of sponsors of their research.*

515  
516 *- Members should strive to avoid bias and the appearance of bias in conducting research, such as in the*  
517 *choice of methods and data inputs, or in the selective reporting of results*

518  
519 *- Members should be aware of conflicts of interest and the appearance of conflicts of interest. As a point*  
520 *of reference, members should look to the rules on disclosure of potential conflicts of interest laid down*  
521 *by major peer-reviewed journals and their own institutions.*

522  
523 *- Members should maintain their professional autonomy and objectivity in conducting and reporting, in*  
524 *writing or verbally, research findings.*

525  
526 *- Methods sections of papers should identify and justify all departures from the a priori analysis plan.*

527  
528 For authors, posting of data and programs is good practice and strongly encouraged whenever  
529 feasible. Best efforts should be made to make them at least available to reviewers when requested,  
530 under confidential arrangements, if necessary. When citing articles in a manuscript, known replicability  
531 of those articles' results should be an important consideration. This is particularly true for those that  
532 are influential to the manuscript's approach or conclusions.

533  
534 Similarly, transparency of data and replicability of research results should be serious considerations for  
535 those organizing conferences, discussing papers, serving on awards or selection committees, writing  
536 promotion or tenure letters, hiring researchers, etc.

## 538 **Scientific Misconduct**

539 Scientific misconduct is the violation of standard codes of scholarly conduct and ethical behavior in

540 professional scientific research. According to the ICMJE<sup>26</sup>, it includes, but is not necessarily limited to:  
541 data fabrication, data falsification including deceptive manipulation of images, and plagiarism. See also  
542 Chapter 8: Publication and Dissemination.

543  
544 The Committee on Publication Ethics (COPE) has developed procedures for editors to follow if there  
545 are concerns about the integrity or conduct of work in submitted or published papers or if scientific  
546 misconduct is suspected. The procedure emphasizes transparency and accountability throughout the  
547 investigation, as well as communication of the whole process. While some may consider failure to  
548 publish clinical trial results or other human studies a form of scientific misconduct, each situation of  
549 alleged misconduct requires individual assessment by relevant stakeholders.

550  
551 *Therefore:*

552  
553 *- Members should maintain and protect the integrity of data used in their studies as well as on any*  
554 *other aspect of their research, as previously discussed (e.g., respect for patient autonomy such as*  
555 *informed consent and data privacy).*

556  
557 *- Members should not draw conclusions beyond or inconsistent with what their data would support and*  
558 *discuss any limitations in a transparent manner.*

## 559 **CHAPTER 6: SPONSORSHIP AND RELATIONSHIPS WITH OTHERS**

560  
561 HEOR sponsors range from life sciences industry and health care insurers to provider and patient  
562 associations and governmental bodies. However, it is understood that much of the funding available to  
563 those who pursue HEOR is provided by bodies with vested interests. A central principle of ISPOR's work  
564 is the maintenance of its own objectivity and autonomy from sponsors and commercial interests.

### 565 **Researchers**

566  
567 Those who conduct HEOR should strive to make the nature, scope, and potential of their work clear to  
568 sponsors. This not only includes being transparent about the kind of knowledge scientific research can  
569 generate but also pertains to the ethical dimension of conducting research. Thus researchers should  
570 make it clear to sponsors that all outputs from a research project will include the acknowledgement of all  
571 sources of funding as part of a conflict of interest declaration.

572  
573 Furthermore, researchers should not only avoid being placed in a position where they experience a  
574 conflict of interest, they should also avoid the appearance of a conflict of interest, and the possibility that  
575 their research will be perceived as biased.

576  
577 When engaging with sponsors, researchers should be clear about the need to maintain their professional  
578 autonomy over all stages of the research, including its design, conduct, and publication. The autonomy  
579 of science contributes to the objectivity of research and, therefore, the authority of the researcher.

580  
581 Sponsors should be informed about the opportunities to enter studies into research registries, as well as  
582 their rights (or lack thereof) of access to - and ownership of - the data generated or collected as part of  
583 the research.

585 When researchers accept sponsorship for a particular project they should be in a position to conduct the  
586 research in a manner that is both timely and reflects the required level of scientific quality and  
587 methodological rigor.

588  
589 HEOR is conducted through close collaboration within teams and between teams, nationally and  
590 internationally. The principle of civility is important to ensure that the contribution from all parties is  
591 respected and understood. Employees and employers have responsibilities to ensure that reputations,  
592 rights, interests of all parties are respected, and that work is done to appropriate standards protecting  
593 proprietary information. Particular care should be taken to ensure that there is no perception of actual  
594 abuse of the relationship between more senior faculty members and students.

595  
596 *Therefore:*

- 597  
598 - *Members should respect the reputations and rights of colleagues when engaged in collaborative*  
599 *projects.*  
600  
601 - *Members should treat their research employees with respect and should compensate them fairly for*  
602 *their work.*  
603  
604 - *Members should protect and promote the interests of their employers, provide competent work,*  
605 *adhering to these broader guidelines, and protect proprietary information.*  
606  
607 - *Members should treat students with respect and refrain from exploiting them under any circumstances.*  
608

### 609 **Responsibility to Sponsors**

610 HEOR must not be used to obtain confidential information about competing products and companies  
611 from participants who are bound by confidentiality agreements with those companies.

612  
613 A researcher may transfer any or all of the researcher's research duties and functions to one or more  
614 subcontractors (e.g., CROs). All parties, including subcontractors, should be contractually bound by the  
615 same legal and ethical requirements as the main researcher.

616  
617 *Therefore:*

- 618  
619 - *Members acting as sponsors should allow HEOR researchers at all times to maintain their scientific*  
620 *integrity and adhere to relevant standards in conducting and reporting research.*  
621  
622 - *Members should respect contractual rights when they agree to perform work for hire and should refrain*  
623 *from disseminating information which they agreed in advance to keep proprietary.*  
624

### 625 **Key Opinion Leaders (KOLs) and Advisory Board Members**

626 The role of KOL brings some ISPOR members into close contact with sponsors. As such, we reiterate  
627 the centrality of independence, professional autonomy and objectivity to the scientific process, including  
628 dissemination of scientific findings.

629  
630 *Therefore:*

631

632 - *When acting as KOLs, ISPOR members should be transparent about payments – and any other*  
633 *benefits - they receive for acting in this capacity.*

634  
635 - *When acting as KOLs, ISPOR members should ensure that the information they are presenting is an*  
636 *accurate representation of the facts available. They should respond to questions and queries honestly*  
637 *and to the best of their abilities.*

638  
639 - *When relying on KOLs, ISPOR members should critically engage with the claims being made. Where*  
640 *appropriate they should seek independent corroboration of any factual claims and consider the full range*  
641 *of alternatives for themselves.*

642  
643 - *When acting as Advisory Board Members, ISPOR members should maintain their independence and*  
644 *professional autonomy and act transparently, e.g., declare conflicts of interest.*

645

### 646 **Responsibility to Research Participants**

647 Researchers should be open and transparent about the aim and objectives of their research, its design,  
648 its conduct and its potential consequences or outcomes. They should be clear with participants about  
649 what is being asked of them, the right to refuse to participate, and the possibilities of withdrawing at a  
650 later date.

651

652 While it might not always be possible, realistic or particularly desirable, researchers should, where  
653 appropriate, aim to communicate results of research to participants. Responsibilities to communicate  
654 aggregated results to participants should be clearly stated in consent materials or processes.

655

656 Informed consent is the tool to ensure that trial participants understand the context and specifics of  
657 clinical trials and/or health care-related research. The informed consent document should be relevant,  
658 easily understandable and practical. It should not serve as a theoretical exercise for the researcher. A  
659 copy of the signed informed consent must be provided to the participant.

660

661 Ethical review of research proposals should, where appropriate, seek input from individuals or  
662 organizations that are able to represent the perspective of patients.

663

664 *Therefore:*

665

666 - *Members should respect the autonomy of research participants in designing and conducting studies,*  
667 *specifically, but not limited to, informed consent and data privacy.*

668

### 669 **IRB/EC Approval**

670 Sponsors should ensure that IRB/EC approval is obtained, as appropriate for the planned research. It is  
671 the responsibility of an IRB/EC to ensure that the rights, safety and well-being of those involved in  
672 research are protected. Furthermore, it should provide public assurance of that protection by, among  
673 other things, reviewing and approving / providing a favorable opinion on the research proposal, the  
674 suitability of the investigator, facilities, and the methods and material to be used in obtaining and  
675 documenting informed consent of research subjects.

676

677 Requirements of the IRB/EC approval shall depend on the research type, study objectives, interaction  
678 with patients and competent authority requirement from different countries. Some recommendations of

679 IRB/EC for different studies appear in Appendix 9. The legal status, composition, function, operations  
680 and regulatory requirements pertaining to independent ethics committees may differ among countries.

681  
682 Appendix 10 provides for involvement of different participants groups, including healthy volunteers,  
683 patients, protected classes, children and vulnerable populations.

## 684 **CHAPTER 7: PATIENT CENTRICITY AND PATIENT ENGAGEMENT IN RESEARCH**

685  
686 The ISPOR Code has been updated to appropriately reflect an increased focus on patient centrality and  
687 patient engagement in research by regulatory and health technology assessment (HTA) agencies, policy  
688 and decision makers, medical technology manufacturers, research organizations, payers and other  
689 stakeholders seeking to understand patients' perspectives and experiences. Organizations support  
690 patient centrality in research for a number of reasons from improved research, utility and efficiency of  
691 clinical trials to ethical concerns and societal and moral obligations. Furthermore, the involvement of  
692 patients or their representatives increases transparency, mutual respect and trust between patients and  
693 other stakeholders, including payers and providers.

694  
695 Reflecting this evolution in the research environment, as an organization, ISPOR has moved to become  
696 more patient-centered. It aligns with ISPOR's members' interests and ISPOR's overall mission to  
697 promote health economics and outcomes research excellence to improve decision making for health  
698 globally. In 2015, the ISPOR Board of Directors unanimously approved a motion to create a special  
699 category of membership within ISPOR for patient representatives to increase patient involvement  
700 throughout ISPOR's activities.

### 701 702 **Understanding Patient Centrality and Patient Engagement**

703 As of 2017, there is no standard definition of patient centrality or patient engagement. Significant  
704 variation exists in how different stakeholders and sectors (e.g., regulators, HTA agencies, the  
705 pharmaceutical industry, academia, hospitals, and patient organizations) define these terms.

706  
707 Patient-centric research should focus on the outcomes that are meaningful and important to patients,  
708 with "those outcomes important to patients' survival, function, or feelings as identified or affirmed by the  
709 patients themselves, or judged to be in patients' best interests by providers and caregivers when  
710 patients cannot report for themselves."<sup>27</sup> In order to understand what is important to patients, they must  
711 be meaningfully engaged in the research from start to finish. Patient-centered outcomes may or may not  
712 be measured by patient self-report<sup>28</sup>.

### 713 714 **Operationalizing Patient Centrality and Patient Engagement**

#### 715 716 *Levels of Patient Engagement*

717 Patient engagement can take many forms. Examples of little or minimal engagement include asking for  
718 patient input by gathering patient reactions and regarding patients as study subjects only. It is low  
719 intensity engagement with unidirectional communication.

720  
721 More meaningful levels of engagement include collaboration and bi-directional communication.  
722 Examples include patient experts in an advisory role providing *a priori* consultation on study design,  
723 procedures and/or outcomes. It is more active, higher-intensity involvement between researcher and  
724 consumer or patient representatives. At the high end of the engagement spectrum is shared leadership  
725 and partnership, characterized by *a priori*, as well as continuous interaction. At this level, patients have

726 a governance role and are paid investigators or consultants. At the highest level of engagement, the  
727 research is patient-driven.

728  
729 There are a number of useful frameworks for patient engagement<sup>29</sup>. They describe (1) patient  
730 involvement through interchange between the patient and provider; (2) the stages of research in which  
731 patients can be involved; and (3) prioritizing stakeholder engagement in research. They serve as a  
732 conceptual basis for patient engagement in medical product development.

733  
734 Researchers should also consider the role of families and family caregivers when taking a patient-  
735 centered approach. Some patients will be unable to engage due to their age or condition. For some  
736 illnesses, there is a significant impact on family life and family caregivers. It is important to include family  
737 and caregiver engagement under these circumstances.

#### 738 739 *Timing of Patient Engagement*

740 Patient input is valuable throughout the medical technology's lifecycle from early development through  
741 dissemination and post-market surveillance. Early and meaningful involvement of knowledgeable  
742 patient representatives and members of patient organizations in setting research questions is highly  
743 recommended. Collaboration with patient organizations as part of the research team is also  
744 encouraged. To accurately capture patients' values and preferences, patients should be involved in  
745 benefit/risk evaluation and related activities throughout the development lifecycle. A planned sequential  
746 approach is recommended where feedback from patients is collected and considered<sup>30</sup>.

747  
748 The patient perspective is especially critical in early phases to determine unmet needs and the correct  
749 study endpoint(s) for medical label claims.<sup>31</sup> Patient input at the study design stage can improve site  
750 selection and recruitment, (e.g. within indigenous or other historically disadvantaged populations), data  
751 collection, and reduce patient burden. Patients (or patient organizations), should actively contribute to  
752 trial documents directed at patients to ensure that the content and format are understood.

753  
754 Patients and patient organizations can also help in the translation of research results by helping to  
755 develop and share lay-person-level summaries of clinical trial results. Finally, patient input is also  
756 needed in assessing real-world effectiveness, cost effectiveness, and value. These assessments should  
757 be enriched with patient input and guided by patient experiences<sup>32</sup>.

#### 758 759 *Partnering with Patient Organizations*

760 Collaboration with patient advocacy organizations can be a sound platform for successful patient  
761 engagement. Researchers will need to familiarize themselves with the many types of organizations that  
762 vary in size and scope (e.g. rare versus high-prevalence diseases; local, regional to international).  
763 They have a range of experiences, organizational cultures, governance structures priorities, and ability  
764 and capacity to engage.

#### 765 766 *Ethical Considerations*

767 Ethical issues often arise in the patient engagement process<sup>33</sup>. Thus, following established protocols  
768 and guidelines is recommended. Rare Diseases Europe (EURORDIS) has published a Charter for  
769 Collaboration between Sponsors and Patient Organizations for Clinical Trials in Rare Diseases<sup>34</sup>. The  
770 European Patients' Academy (EUPATI) has developed guidance for stakeholders as well<sup>35</sup>.

771  
772 A research contract between patients and research partners is also recommended, even if patients are  
773 driving the research themselves. The contract should be respectful and clearly outline roles and  
774 deliverables. The contract should recognize patients as experts in their health condition and compensate

775 them appropriately. Further information on written agreements and compensation are available from  
776 EUPATI<sup>36</sup>, PCORI<sup>37</sup> and the European Federation of Pharmaceutical Industries and Associations  
777 (EFPIA)<sup>38</sup>.

778  
779 Researchers should recognize that patients are not trained researchers. Researchers should recognize  
780 patients' input in framing research questions and selecting correct methods for study conduct versus  
781 driving the research methodological or analytical approach. However, patients' opinions should be  
782 included throughout in the research lifecycle.

783  
784 *Therefore,*

785  
786 *- Stakeholder input, including patients (and representatives of patients such as family caregivers and*  
787 *advocacy organizations) in study development, can strengthen the study design and utility:*

788  
789 *- Patient input is valuable throughout the research lifecycle from early development to*  
790 *dissemination and post-marketing surveillance.*

791  
792 *- Researchers should involve patients and their representatives as partners before, during, and*  
793 *after conducting research.*

794  
795 *- To prevent or address ethical issues arising in the patient engagement process, following established*  
796 *protocols and guidelines is recommended.*

## 797 **CHAPTER 8: PUBLICATION AND DISSEMINATION**

798  
799 The main purpose of publishing, or otherwise disseminating HEOR, is to provide reliable and relevant  
800 information related to health care treatments and programs. Therefore, it is important that members  
801 submitting manuscripts ensure that these contain no inaccuracies, nor misrepresent the data.  
802 Publications can discuss methodological principles, the results of empirical studies, or policy choices.  
803 The main users of HEOR include decision makers concerned with population-based choices, health  
804 professionals deciding on treatment options, and patients wishing to understand more about the  
805 treatments available.

### 806 **Scientific Misconduct: Plagiarism**

807  
808 Plagiarism - the act of passing off as one's own any writing, verbatim or paraphrased, that which was  
809 authored by another - is perhaps the most fundamental ethics violation for any author in any field of  
810 endeavor. Copyright laws protect writers' words as their legal property. Furthermore, it is extremely  
811 important to give comprehensive citations in order to avoid unintentional plagiarism.

812  
813 In the health and medical sciences, including HEOR, there is a gray area as to what constitutes  
814 plagiarism in the context of an individual author publishing new work that is similar in many respects to  
815 prior work on which he or she was one of several authors. On occasion, an author is invited to submit a  
816 special article or book chapter due to prior participation in an area of important research with the  
817 expectation that their contribution will derive from the prior work. In these instances, it is important that  
818 the author double-check to make sure that no written material (or tables or figures) is being replicated  
819 from the earlier work without permission from the copyright holder.

820

In addition, ISPOR initiated a scientific and health policy group publication rule that “No member of an ISPOR Task Force or Special Interest Group should publish any material from an upcoming report, public presentation, or project deliverable without first consulting the larger group for permission prior to submission and publication.”

Therefore:

- Members should not engage in any act of plagiarism, including self-plagiarism.
- Members should not publish any material relating to the activities of an ISPOR Task Force, Special Interest Group or other ISPOR group at any stage, without first consulting fellow group members / co-authors for permission.

See chapter 5 for more on scientific misconduct.

### **Bias**

A key concern in publication and dissemination is the possibility of bias, either *publication bias*, whereby studies with negative or inconclusive results tend not to be published, or *analytic bias*, whereby analysts make inappropriate methodological choices that favor one treatment option over another. Bias is a particularly pertinent concern in the field of HEOR, where a high proportion of studies are sponsored and where the analyst often has considerable discretion in the choice of methods and assumptions.

ISPOR has published more than 50 Good Practices for Outcomes Research Reports on conducting outcomes research (clinical, economic or patient-reported) or using outcomes research in health care decisions. (Please see ISPOR Good Practices for Outcomes Research Index, [https://www.ispor.org/workpaper/practices\\_index.asp](https://www.ispor.org/workpaper/practices_index.asp)) While these reports do not address ethical principles directly, the specification of good research methods is an important component of recognizing and eliminating analytic bias.

The main method of disseminating HEOR is through peer-reviewed journals. Therefore, a major source of ethical principles and good publishing practice is the recommendations of the ICMJE<sup>39</sup>, which have the endorsement and support of all the major clinical and health services research journals (ICMJE, 2016). The recommendations for ISPOR members in this chapter are consistent with those of the ICMJE but offer more details relevant to this particular field of research.

### **Freedom to Publish the Findings without Restrictions**

Both peer-reviewed journals and the users of HEOR take an interest in the nature of the relationship between the researcher and the sponsor, as this is one indicator of the likelihood of any bias in the research. This relationship is usually expressed through a contract between the researcher and sponsor. In negotiating the contract, researchers should pay particular attention to the need for transparency throughout the research process and the freedom to publish the findings without restrictions<sup>40</sup>.

Members should seek to establish, in advance, a clear agreement with the sponsor on whether the results of a given piece of work can be published or presented. This could include statements on whether the sponsor has a right to review or approve any manuscript prior to publication and on which party has the intellectual property rights in the outputs of the research. It is important to specify publication rights, one way or the other, in the contract. University contracts usually do specify and generally a university will not sign off on a contract that allows the sponsor to disallow publication. Prior review and comment is generally accepted by universities. Individual researchers or vendors may be willing to do “work for hire” which does not guarantee publication rights; in such a case, if anything is

published, it should be disclosed that publication rights were not guaranteed in advance. Considerations where preventing publication would not be acceptable in any case could include revelations of safety issues, in which failure to disclose could result in a public health hazard.

Therefore:

*- In the case of sponsored research, members should agree to a contract that clearly sets out their rights, and those of the sponsor (e.g., intellectual property rights and rights to publish), in the conduct and reporting of the study. The nature of this agreement should be summarized in the published paper.*

### **Transparency in Reporting**

Transparency in reporting is also essential to reduce the possibility of bias in research. Several reporting guidelines exist, including those developed by CONSORT for clinical research (including quality of life measurement)<sup>41 42 43 44</sup> and STROBE for observational studies<sup>45</sup>. High-quality reporting also aids the peer-review process, although journal editors and reviewers may also ask for access to the original data, the statistical analyses performed, or the models used in the research.

Authors of publications should endeavor to respond as fully as possible to requests for additional information on their data or methods. Offering full access to data, analyses and models represents a level of transparency that can enhance the credibility of the research. However, access to some data may be restricted by contractual obligations, proprietary reasons, IRB restrictions or the general need to protect the privacy of participants in the research. Also allowing access to executable electronic copies of models has raised specific concerns on the part of researchers who fear that their intellectual capital could be undermined if the model were copied<sup>46</sup>.

On the other hand, peer reviewers and journal editors may feel that access is required in order to adequately verify the quality of the research. Researchers should remember that peer reviewers are already bound by confidentiality agreements, and some journals have strengthened these in order to reassure authors that the intellectual capital in their work will be protected.

It was mentioned in Chapter 4 that the registration of the clinical study alongside which a HEOR is conducted can be a key element in ensuring the transparency of research, therefore:

*- Where a HEOR study is being conducted alongside a clinical study gathering data prospectively (such as a clinical trial or observational study) members should report whether the clinical study concerned has been registered on ClinicalTrials.gov, Registry of Patient Registries (patientregistry.ahrq.gov), ENCePP e-Register of Studies<sup>47</sup>, or equivalent databases of studies in their own country or region.*

Where research is disseminated in non-peer-reviewed journals or through electronic media, such as websites or social media, the scrutiny of peer review does not generally exist (although comments sections on web posts might be considered an informal peer review). The way in which researchers should approach this depends on whether they are purporting to report fact or opinion—unless it is clear that mere opinions are being expressed, authors should be willing to offer the same level of access to underlying data and/or analyses as they would to journal peer reviewers.

### **Study Authorship**

The named authors formally take responsibility for the report of the research. Therefore, some study users view the identity of the authors as one indicator of the likely quality and reliability of the research, although when acting as editors or reviewers of papers for journals, ISPOR members should make

919 judgments based solely on the quality of the research, not the identity or affiliations of the authors (if  
920 these are not already anonymized by the journal concerned)

921  
922 Authorship also provides recognition of the researchers' contribution. Therefore, it is wrong to include an  
923 author who did not make a substantive contribution due to their name recognition and perceived status.  
924 Similarly, it is wrong to exclude an individual who had made a substantial contribution because of their  
925 affiliation. Criteria include:

- 926 1) Substantial contributions to the conception or design of the work; or the acquisition, analysis or  
927 interpretation of data for the work; AND
- 928 2) Drafting of the work or revising it critically for important intellectual content; AND
- 929 3) Final approval of the version to be published; AND
- 930 4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the  
931 accuracy or integrity of any part of the work are appropriately investigated and resolved<sup>48</sup>

932  
933  
934 Other individuals participating in the research, but not qualifying as authors, should be acknowledged.

935  
936  
937 In addition, the ICMJE and many peer-reviewed journals require the corresponding author to confirm  
938 that these conditions have been met. Specific journals such as JAMA have guidelines, and these are  
939 very useful generally.

940  
941 Journals now generally require individual authors of a manuscript to certify by signature that they have  
942 contributed sufficiently to be listed as an author. However, journals vary in their requirements for  
943 certification so ISPOR, as an organization, encourages its members to adhere to fair and equitable  
944 requirements for authorship and to respect their colleagues in the process.

#### 945 **Financial Disclosure, Conflicts of Interest and Past Work Relationships**

946 Another important condition of authorship is that individuals disclose any financial and/or other  
947 relationships that may be perceived to be conflicts of interest with respect to the work being reported. In  
948 the field of HEOR, it is particularly important to disclose any present or past relationships with the  
949 manufacturers of any products referred to in the research or any competitor products.

950  
951  
952 In reporting past relationships, many researchers will have a large number of such relationships  
953 stretching back over a number of years. A common time frame is to report any relationships within the  
954 past three years<sup>49</sup>, but different journals have different guidelines. The ICMJE specifies no limit.

955  
956 *Therefore:*

957  
958 - *Members should endeavor to publicly disseminate their work and to publish it in peer-reviewed journals*  
959 *when possible.*

960  
961 - *Members should work, where appropriate, to encourage the establishment and/or maintenance of an*  
962 *appropriate peer review process that examines the quality of the methodological rigor independently of*  
963 *the organization for which the individual works.*

964  
965 - *Members serving as peer reviewers for journals should respect the confidentiality of the material under*  
966 *review and understand that their access to it is solely for the purposes of performing the review.*

967

- 968 - *The description of study methods (design, study setting, data sources and input values, sampling and*  
969 *analyses) should be complete and transparent enough for a suitably trained researcher to replicate the*  
970 *study.*
- 971
- 972 - *Methods sections of papers should give thorough, transparent attention to all measures taken to*  
973 *minimize bias.*
- 974
- 975 - *Where allowable by law and IRB approval, members should respond favorably to requests from journal*  
976 *editors and reviewers for access to original data and electronic copies of models where this access is*  
977 *required to ensure a rigorous peer review process and where commercial-in-confidence arrangements*  
978 *can be maintained.*
- 979
- 980 - *In those instances in which study methods include analysis of a database (retrospective or*  
981 *prospective), members should describe approaches, methods, technologies used to ensure data*  
982 *completeness, and validity as well as the software package(s) used for data analysis. Members should*  
983 *have the education, training, and experience to perform the assigned tasks.*
- 984
- 985 - *In those instances in which sharing of model(s) and/or data source(s) is not feasible, members should*  
986 *be encouraged to provide supporting material demonstrating model and/or data validity, such as range*  
987 *and logic checks, and assessment of data completeness.*
- 988
- 989 - *If submitting to a journal or publication that does not have peer review, or disseminating a report via*  
990 *electronic media, members should avoid the inclusion of material that is overly technical and/or cannot*  
991 *be supported by basic article references, or make it clear that the article represents the author's own*  
992 *opinion. If research is being reported, then access to the underlying data and/or analyses should be*  
993 *offered in the same manner as would be done under a peer-review process.*
- 994
- 995 - *Members should never intentionally plagiarize another author's work and if publishing work similar to*  
996 *anything jointly authored with others should ensure that no replication of the prior work was*  
997 *unintentionally done.*

## 998 **CHAPTER 9: CONCLUSION AND LIMITATIONS**

999

1000 ISPOR recognizes that within the fast changing climates of different health care systems, it is difficult to  
1001 address all ethical issues HEOR practitioners face. New data sources might emerge; genomic  
1002 sequencing and Internet of Things might make privacy almost impossible to protect; and open data  
1003 might pose new challenges to intellectual property rights.

1004

1005 Nevertheless, ISPOR recognizes that its activities and those of its members affect a number of  
1006 constituencies, and there may be conflicting standards of professional conduct. Patients as stakeholders  
1007 and patient engagement are two relatively new concepts impacting health care research, especially in  
1008 Europe and North America. While the impact of this much needed social movement is slowly starting to  
1009 become clearer, its relevance and impact on ISPOR members, especially researchers, requires further  
1010 elucidation and guidance. This Code, however, cuts across virtually all areas of research and  
1011 dissemination and is meant to be a comprehensive guide for HEOR researchers.

1012

1013

1014

DO NOT COPY

1016  
1017 **ISPOR CODE OF ETHICS 2017 SUMMARY POINTS**

1018  
1019 **CHAPTER 1: INTRODUCTION**

- 1020  
1021 1. *ISPOR should publicize this Code of Ethics to members and non-members involved in*  
1022 *pharmacoeconomics and outcomes research.*
- 1023 2. *ISPOR should strive for a balance in sponsorship of its conferences and other activities*  
1024 *by providing decision criteria for accepting of funding and ensuring full transparency,*  
1025 *thereby avoiding the appearance of bias or conflict of interest.*
- 1026 3. *Because, as a practical matter, most funding will come from different entities, ISPOR*  
1027 *should continue to maintain its own statement of objectivity and autonomy.*
- 1028 4. *ISPOR should strive to assure that its journal, Value in Health, only publishes papers*  
1029 *that have gone through a rigorous peer- review process.*
- 1030 5. *ISPOR should have a Board of Directors that is representative of the various*  
1031 *constituencies the Society serves.*
- 1032 6. *The ISPOR program planning and selection committees should have membership*  
1033 *representative of all of its major constituencies.*
- 1034 7. *Like other professional societies, ISPOR should be conscious of broader ethical issues*  
1035 *impacting on global and regional medical resource allocation, public health policies and*  
1036 *the global healthcare environment, and the research side on topics such as patient*  
1037 *autonomy and research conduct. These issues include but are not limited to: prejudice,*  
1038 *equity in healthcare delivery and access.*

1039  
1040 **CHAPTER 2: APPLICATION OF ETHICAL PRINCIPLES TO THE ISPOR CODE**

- 1041  
1042 8. *Members should maintain a current knowledge of research practices, with due*  
1043 *consideration of those practices most relevant to the research that is being done in their*  
1044 *own countries.*
- 1045 9. *Privacy: Members who work in HEOR can be privy to data sources containing protected*  
1046 *health information (PHI) and other personal data from patients. It is essential that these*  
1047 *data are handled with utmost care so that patient confidentiality can be maintained at all*  
1048 *times and no breaches to patient privacy occur.*
- 1049 10. *Transparency and Integrity: Members must disclose research methods in sufficient detail*  
1050 *to permit replication. The funding sources should be clearly acknowledged, and any*  
1051 *conflicts of interests declared. Designing, conducting and especially reporting of the*  
1052 *study should be an unbiased reflection of the full range of findings generated.*

1053 *11. Civility: Members' research and discussion should respect the dignity of all participants,*  
1054 *including patients and providers of care. It is also a responsibility to treat fellow*  
1055 *researchers with respect.*

1056  
1057 **CHAPTER 3: SCOPE OF THE CODE**

1058  
1059 *12. Members should adhere to the standards of practice for their respective fields of*  
1060 *research and identify any official guidelines and standards used.*

1061  
1062 **CHAPTER 4: RESEARCH DESIGN CONSIDERATIONS**

1063  
1064 *13. When recruiting patients for a study, from the point of "first contact" researchers should*  
1065 *be open about their intentions and how the research is funded, and should provide*  
1066 *potential subjects with the information mandated in their proposals as reviewed by*  
1067 *research ethics committees.*

1068  
1069 *14. Members should describe the analytic population in terms of persons, geography, time*  
1070 *period and selection criteria. Members should choose, and obtain permissions to use a*  
1071 *suitable research setting and/or existing data or literature to provide information about a*  
1072 *specific patient population to which the study results are meant to apply. The number of*  
*sites selected for a study should be appropriate to meet the research objectives.*

1073  
1074 *15. Safety and adverse events reporting (AER) are important aspects of all primary research*  
1075 *involving patients and medical interventions, are applicable to many HEOR activities,*  
*and must follow international guidelines.*

1076  
1077 *16. The balance of risk or harm to benefit for patients must be considered in HEOR studies,*  
*and must be communicated to patients via informed consent.*

1078  
1079 *17. While an 'incentive', honorarium or remuneration is often necessary to recruit participants*  
1080 *into a research study, researchers must ensure that the incentive would not induce*  
1081 *participants to accept risks they would not be willing to accept if they were offered a*  
1082 *smaller or no incentive. Any such proposed payments are subject to providers' internal*  
1083 *compliance guideline and IRB/EC approval, and must be detailed in the research*  
*proposal submitted for review.*

1084  
1085 *18. When using secondary data sources initially collected for another purpose, HEOR*  
1086 *researchers should ensure that intellectual property rights are respected and that all the*  
*appropriate permissions have been secured.*

1087  
1088 *19. Given the potential for bias in the analysis of secondary data, the most important general*  
*ethical principles are those of 'reasonableness' and 'transparency'.*

1089  
1090 *20. While registration of observational studies is generally not required at this time, members*  
1091 *are encouraged to register such studies prospectively to recognize ethical obligations to*  
*patients and to avoid the potential for publication bias.*

- 1092 *21. When study methods include analysis of a database, members should describe*  
1093 *approaches, methods, technologies used to ensure data completeness and validity as*  
1094 *well as the software package(s) used for data analysis. Members should have the*  
1095 *education, training and experience to perform the assigned tasks.*
- 1096 *22. Where a HEOR study is being conducted alongside a clinical study gathering data*  
1097 *prospectively (such as a clinical trial or observational study), where possible members*  
1098 *should ensure that the clinical study concerned has been registered on*  
1099 *ClinicalTrials.gov, Registry of Patient Registries (patientregistry.ahrq.gov), ENCePP*  
1100 *(European Network of Centres for Pharmacoepidemiology and Pharmacovigilance) e-*  
1101 *Register of Studies<sup>†</sup>, or equivalent database in their own country.*
- 1102 *23. In conducting modeling studies, members should: ensure that the input parameters are*  
1103 *estimated based on a comprehensive review of the available literature; be transparent*  
1104 *about the estimates they use for key parameters; provide the logic they used in selecting*  
1105 *particular estimates; and explore the impact of their choices through sensitivity analysis.*

1106  
1107 **CHAPTER 5: DATA CONSIDERATIONS**  
1108

- 1109 *24. When a database (from primary data collection and/or secondary data use) is analyzed,*  
1110 *members should provide a description of approaches, tools and technologies used to*  
1111 *store the data and maintain patient privacy/confidentiality and de-identification.*
- 1112 *25. Personal data should be maintained securely and adequate back-up should be*  
1113 *maintained. Data access should be limited to authorized individuals. Control systems*  
1114 *should be put in place to ensure authenticity, integrity and confidentiality of data records*  
1115 *when transmitted electronically.*
- 1116 *26. Researchers should offer the maximum level of access to the anonymized, group-level*  
1117 *data used in their research. If data access is restricted by proprietary or contractual*  
1118 *considerations, those considerations should be disclosed. If journal reviewers deem it*  
1119 *important that statistical review of proprietary data be conducted, authors should work*  
1120 *with both the data owners and the reviewers to find appropriate confidential*  
1121 *arrangements for such review whenever feasible.*
- 1122 *27. Members' hypotheses and research designs should be defined a priori, reported*  
1123 *transparently, defended relative to alternatives, and planned to recognize and minimize*  
1124 *all types of bias.*
- 1125 *28. Members should fully disclose the identity of sponsors of their research.*
- 1126 *29. Members should strive to avoid bias and the appearance of bias in conducting research,*  
1127 *such as in the choice of methods and data inputs, or in the selective reporting of results*
- 1128 *30. Members should be aware of conflicts of interest and the appearance of conflicts of*

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<sup>†</sup> [encepp.eu/encepp/studiesDatabase.jsp](http://encepp.eu/encepp/studiesDatabase.jsp)

1129 *interest. As a point of reference, members should look to the rules on disclosure of*  
1130 *potential conflicts of interest laid down by major peer-reviewed journals and their own*  
1131 *institutions.*

1132 *31. Members should maintain their professional autonomy and objectivity in conducting and*  
1133 *reporting, in writing or verbally, research findings.*

1134 *32. Methods sections of papers should identify and justify all departures from the a priori*  
1135 *analysis plan.*

1136 *33. Members should maintain and protect the integrity of data used in their studies as well*  
1137 *as on any other aspect of their research, as previously discussed (e.g. respect for*  
1138 *patient autonomy such as informed consent and data privacy).*

1139 *34. Members should not draw conclusions beyond or inconsistent with what their data would*  
1140 *support and discuss any limitations in a transparent manner.*

1141  
1142 **CHAPTER 6: SPONSORSHIP AND RELATIONSHIPS WITH OTHERS**  
1143

1144 *35. Members should respect the reputations and rights of colleagues when engaged in*  
1145 *collaborative projects*

1146 *36. Members should treat their research employees with respect and should compensate*  
1147 *them fairly for their work.*

1148 *37. Members should protect and promote the interests of their employers, provide competent*  
1149 *work, adhering to these broader guidelines, and protect proprietary information.*

1150 *38. Members should treat students with respect and refrain from exploiting them under any*  
1151 *circumstances.*

1152 *39. Members acting as sponsors should allow HEOR researchers at all times to maintain*  
1153 *their scientific integrity and adhere to relevant standards in conducting and reporting*  
1154 *research.*

1155 *40. Members should respect contractual rights when they agree to perform work for hire and*  
1156 *should refrain from disseminating information which they agreed in advance to keep*  
1157 *proprietary.*

1158 *41. When acting as key opinion leaders (KOLs), ISPOR members should be transparent*  
1159 *about payments – and any other benefits - they receive for acting in this capacity.*

1160 *42. When acting as KOLs, ISPOR members should ensure that the information they are*  
1161 *presenting is an accurate representation of the facts available. They should respond to*  
1162 *questions and queries honestly and to the best of their abilities.*

1163 *43. When relying on KOLs, ISPOR members should critically engage with the claims being*  
1164 *made. Where appropriate they should seek independent corroboration of any factual*  
1165 *claims and consider the full range of alternatives for themselves.*

1166 44. *When acting as Advisory Board Members, ISPOR members should maintain their*  
1167 *independence and professional autonomy and act transparently, e.g., declare conflicts of*  
1168 *interest.*

1169 45. *Members should respect the autonomy of research participants in designing and*  
1170 *conducting studies, specifically but not limited to informed consent and data privacy.*

1171  
1172 **CHAPTER 7: PATIENT ENGAGEMENT**  
1173

1174 46. *Stakeholder input including patients (and representatives of patients such as family*  
1175 *caregivers and advocacy organizations) in study development, can strengthen the study*  
1176 *design and utility.*

1177  
1178 a. *Patient input is valuable throughout the medical product lifecycle from early*  
1179 *development to dissemination and post-marketing surveillance.*

1180  
1181 b. *Researchers should involve patients and their representatives as partners before,*  
1182 *during, and after conducting research.*

1183  
1184 47. *To prevent or address ethical issues arising in the patient engagement process, following*  
1185 *established protocols and guidelines is recommended.*

1186  
1187 **CHAPTER 8: PUBLICATION AND DISSEMINATION**  
1188

1189 48. *Members should not engage in any act of plagiarism. Members should not publish any*  
1190 *material relating to the activities of an ISPOR Task Force, Special interest Group or other*  
1191 *ISPOR group without first consulting fellow group members for permission*

1192 49. *In the case of sponsored research, members should agree to a contract that clearly sets*  
1193 *out their rights, and those of the sponsor (e.g. intellectual property rights and rights to*  
1194 *publish), in the conduct and reporting of the study. The nature of this agreement should*  
1195 *be summarized in the published paper.*

1196 50. *Where a HEOR study is being conducted alongside a clinical study gathering data*  
1197 *prospectively (such as a clinical trial or observational study), members should report*  
1198 *whether the clinical study concerned has been registered on ClinicalTrials.gov, Registry*  
1199 *of Patient Registries (patientregistry.ahrq.gov), ENCePP e-Register of Studies, or*  
1200 *equivalent database in their own country.*

1201 51. *Members should endeavor to publicly disseminate their work and to publish it in peer-*  
1202 *reviewed journals when possible.*

1203 52. *Members should work, where appropriate, to encourage the establishment and/or*  
1204 *maintenance of an appropriate peer review process that examines the quality of the*  
1205 *methodological rigor independently of the organization for which the individual works.*

1206 53. *Members serving as peer reviewers for journals should respect the confidentiality of the*  
1207 *material under review and understand that their access to it is solely for the purposes of*  
1208 *performing the review.*

1209 54. *The description of study methods (design, study setting, data sources and input values,*  
1210 *sampling and analyses) should be complete and transparent enough for a suitably*  
1211 *trained researcher to replicate the study.*

1212 55. *Methods sections of papers should give thorough, transparent attention to all measures*  
1213 *taken to minimize bias.*

1214 56. *Members should respond favorably to requests from journal editors and reviewers for*  
1215 *access to original data and electronic copies of models where this access is required to*  
1216 *ensure a rigorous peer review process and where commercial-in-confidence*  
1217 *arrangements can be maintained.*

1218 57. *In those instances in which study methods include analysis of a database (retrospective*  
1219 *or prospective), members should describe approaches, methods, technologies used to*  
1220 *ensure data completeness, and validity as well as the software package(s) used for data*  
1221 *analysis. Members should have the education, training and experience to perform the*  
1222 *assigned tasks.*

1223 58. *In those instances in which sharing of model(s) and/or data source(s) is not feasible,*  
1224 *members should be encouraged to provide supporting material demonstrating model*  
1225 *and/or data validity, such as range and logic checks, and assessment of data*  
1226 *completeness.*

1227 59. *If submitting to a journal or publication that does not have peer review, or disseminating*  
1228 *a report via electronic media, members should avoid the inclusion of material that is*  
1229 *overly technical and/or cannot be supported by basic article references, or make it clear*  
1230 *that the article represents the author's own opinion. If research is being reported, then*  
1231 *access to the underlying data and/or analyses should be offered in the same manner as*  
1232 *would be done under a peer-review process.*

1233 60. *Members should discourage, where possible, listing of an author on any publication*  
1234 *where the individual has not performed substantial work. As a point of reference,*  
1235 *members should look to the checklists provided by major peer reviewed journals to*  
1236 *assist them in deciding inclusion of authors.*

1237  
1238 61. *Any contributor to a report or publication should disclose any current or past*  
1239 *relationships with a company or competitor of any product discussed in the work.*

1240 62. *Members should never intentionally plagiarize another author's work and if publishing*  
1241 *work similar to anything jointly authored with others should ensure that no replication of*  
1242 *the prior work was unintentionally done.*

## 1243 **CHAPTER 9: CONCLUSIONS AND LIMITATIONS**

1244 No summary points included

**ISPOR CODE OF ETHICS 2017 GLOSSARY**

- 1245  
1246  
1247 **AER** – Adverse Event Reporting  
1248 **AHRQ** – Agency for Healthcare Research and Quality  
1249 **APPI** – The Act on the Protection of Personal Information  
1250 **CMS** – Center for Medicare and Medicaid Services  
1251 **CONSORT** - Consolidated Standards of Reporting Trials  
1252 **COPE** – Committee on Publication Ethics  
1253 **CRO** – Clinical Research Organization  
1254 **EC** – Ethics Committee or Research Ethics Committee  
1255 **EFPIA** – European Federation of Pharmaceutical Industries and Associations  
1256 **ENCePP** – European Network of Centres for Pharmacoepidemiology and Pharmacovigilance  
1257 **GDPR** – General Data Protection Regulation  
1258 **HEOR** – Health Economics and Outcomes Research  
1259 **HIPAA** – Health Insurance Portability and Accountability Act  
1260 **HTA** – Health Technology Assessment  
1261 **ICH GCP** – International Conference on Harmonization Good Clinical Practice  
1262 **ICJME** – International Committee of Medical Journal Editors  
1263 **IoT** – Internet of Things  
1264 **IRB** – Internal Review Board  
1265 **KOL** – Key Opinion Leader  
1266 **PHI** – Protected Health Information  
1267 **REC** – Ethics Committee or Research Ethics Committee  
1268 **SEER** – Surveillance, Epidemiology and End Results  
1269 **SNIIRAM** – Systeme National d’Information Inter Regimes de l’Assurance Maladie  
1270 **STROBE** - STrengthening the Reporting of OBServational studies in Epidemiology.  
1271 **TPP** – Target Patient Profile  
1272 **UK HES** – United Kingdom Hospital Episode Statistics  
1273

## REFERENCES

- <sup>1</sup> International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Code of Ethics (2008). Available from: <https://www.ispor.org/workpaper/CodeOfEthics.asp>
- <sup>2</sup> Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects (1964-2013), World Medical Association. Available from: [http://www.up.ac.za/media/shared/Legacy/sitefiles/file/45/2875/declarationofhelsinki\\_fortaleza\\_brazil2013.pdf](http://www.up.ac.za/media/shared/Legacy/sitefiles/file/45/2875/declarationofhelsinki_fortaleza_brazil2013.pdf)
- <sup>3</sup> Sanders GD, Neumann PJ, Basu A, et al. (Eds.) Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses Second Panel on Cost-Effectiveness in Health and Medicine. *JAMA*. 2016;316(10):1093-1103
- <sup>4</sup> Berger ML, Binglefors K, Hedblom EC, Pashos CL, Torrance GW. (eds). Health Care Cost, Quality, and Outcomes: ISPOR Book of Terms. Lawrenceville, NJ: ISPOR, 2003.
- <sup>5</sup> Good Clinical Practice (GCP) Available from: <http://ichgcp.net/>
- <sup>6</sup> European Medicines Agency (EMA). Guideline on good pharmacovigilance practices (GVP), Module VIII – Post-authorization safety studies (Rev 2). Doc Ref. EMA/813938/2011. 4 August 2016. Available from: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2012/06/WC500129137.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129137.pdf)
- <sup>7</sup> Directive 2010/84/EU of the European Parliament and of the Council (15 Dec 2010). Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:348:0074:0099:EN:PDF>
- <sup>8</sup> American Academy of Otolaryngology – Head and Neck Surgery, Surveillance, Epidemiology and End Results (SEER). Available from: <http://www.entnet.org/content/surveillance-epidemiology-and-end-results-seer-medicare>
- <sup>9</sup> Hospital Episodes Statistics (HES) Available from: <http://digital.nhs.uk/hesdata>
- <sup>10</sup> Système National d'Informations Inter Régimes de l'Assurance Maladie (SNIIRAM) (French: National Information System Inter Plans Health Insurance). Available from: <http://www.ameli.fr/>
- <sup>11</sup> Daniels N. Accountability for reasonableness: an update, *BMJ* 2000;321:1300-1301
- <sup>12</sup> Parmenter, L. US and European Perspectives on Interventional and Observational Research Designs in Post-Marketing Safety. *Applied Clinical Trials* (2012) Available from: <http://www.appliedclinicaltrials.com/us-and-european-perspectives-interventional-and-observational-research-designs-post-marketing-safety>
- <sup>13</sup> Food & Drug Administration (FDA). Observational Research Exhibit 18. Available from: <http://www.fda.gov/ohrms/dockets/dockets/05p0224/05p-0224-cp00001-Exhibit-18-Observational-Research-vol1.pdf> [Accessed: May 2017]
- <sup>14</sup> Williams RJ, Tse T, Harlan WR, Zarin DA. Registration of observational studies: Is it time?. *CMAJ*. 2010 Oct 19;182 (15):1638-42. doi: 10.1503/cmaj.092252. Epub 2010 Jul 19. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2952011/pdf/1821638.pdf> [Accessed February 2016]
- <sup>15</sup> European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) EU electronic Register of Post-Authorisation Studies (EU PAS Register). Available from: <http://encepp.eu/encepp/studiesDatabase.jsp>
- <sup>16</sup> International Society for Pharmacoeconomics and Outcomes Research (ISPOR). ISPOR Good Practices for Outcomes Research Index. Available from: [http://www.ispor.org/workpaper/practices\\_index.asp](http://www.ispor.org/workpaper/practices_index.asp). [Accessed May 17, 2017]
- <sup>17</sup> Caro et al, Modeling good research practices - overview: A report of the ISPOR-SMDM modeling good research practices task force-1. *Value Health* 2012;15:796-803
- <sup>18</sup> Eddy DM, Hollingworth W, Caro JJ, et al. Model transparency and validation: A report of the ISPOR-SMDM modeling good research practices task force-4. *Value Health* 2012;15:843-50.
- <sup>19</sup> Briggs AH, Weinstein MC, Fenwick E, et al. Model parameter estimation and uncertainty analysis: A report of the ISPOR-SMDM modeling good research practices task force-6. *Value Health* 2012;15:835-42
- <sup>20</sup> Esposito D, ed. Reliability and Validity of Data Sources for Outcomes Research & Disease and Health Management Programs. Lawrenceville, NJ: ISPOR, 2013
- <sup>21</sup> General Data Protection Regulation (GDPR), European Commission. (2016) Available from: <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679&qid=1462359521758&from=EN> [Accessed May, 16 2017]
- <sup>22</sup> US Health & Human Services Health Insurance Portability and Accountability Act (HIPAA), US Department of Health & Human Services (1999, 2002) Available from: <http://www.hhs.gov/hipaa/> [Accessed May, 16 2017]
- <sup>23</sup> The Act on the Protection of Personal Information, Act No. 57 of (2003) Available from: <http://www.cas.go.jp/jp/seisaku/hourei/data/APPI.pdf> [Accessed May, 16 2017]
- <sup>24</sup> Cochrane J. Secret Data – the Grumpy Economist (Dec 2015) Available from: [http://johnhcochrane.blogspot.co.uk/2015/12/secret-data.html?utm\\_source=feedburner&utm\\_medium=email&utm\\_campaign=Feed:+TheGrumpyEconomist+\(The+Grumpy+Economist\)](http://johnhcochrane.blogspot.co.uk/2015/12/secret-data.html?utm_source=feedburner&utm_medium=email&utm_campaign=Feed:+TheGrumpyEconomist+(The+Grumpy+Economist))
- <sup>25</sup> International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Value in Health Policies. Available from: <http://www.ispor.org/publications/value/policies.asp> [Accessed May 17, 2017]

- <sup>26</sup> International Committee of Medical Journal Editors (ICMJE), Scientific Misconduct, Expressions of Concern, and Retraction. Available from: <http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/scientific-misconduct-expressions-of-concern-and-retraction.html> [Accessed May 17 2017]
- <sup>27</sup> Patrick D. What Does "Patient-Centered Outcomes" Mean? Presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 18th Annual Meeting; New Orleans, May 18, 2013.
- <sup>28</sup> Perfetto E and L Burke. Criteria for Successful Patient Engagement: An Essential Part of Patient-Focused Drug Development. Presented at the the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 3rd Patient Representatives Roundtable, May 15, 2015
- <sup>29</sup> Carman et al., Domecq et al., Guise et al., Shippee et al., Perfetto 2015, M-CERSI 2015, Clinical Trials Transformation Initiative (CTTI)
- <sup>30</sup> Smith, Sophia K.; Wendy Selig; Matthew Harker; Jamie N. Roberts; Sharon Hesterlee; David Leventhal; Richard Klein; Bray Patrick-Lake; Amy P. Abernethy, 'Patient Engagement Practices in Clinical Research among Patient Groups', Industry, and Academia in the United States: A Survey. PLOS ONE October 14, 2015
- <sup>31</sup> Walton MK, Powers JA, Hobart J, et al. Clinical outcome assessments: A conceptual foundation – Report of the ISPOR Clinical Outcomes Assessment Emerging Good Practices Task Force. Value Health 2015; 18:741-52.
- <sup>32</sup> NHC Value Model Rubric, NICE patient input in HTA
- <sup>33</sup> Patient Centered Outcomes Research Institute (PCORI). Engagement Rubric for Applicants (2016) Available from: <http://www.pcori.org/sites/default/files/Engagement-Rubric.pdf> [Accessed May 17 2017]
- <sup>34</sup> Eurordis Rare Disease Europe. The Eurordis Charter in Practice. Available from: [http://www.eurordis.org/IMG/pdf/Charter\\_Clinical\\_Trials-Final.pdf](http://www.eurordis.org/IMG/pdf/Charter_Clinical_Trials-Final.pdf) [Accessed May 17 2017]
- <sup>35</sup> European Patients Academy (EUPATI). Guidance for Patient Involvement in Industry-led Medicines R&D. Available from: <https://www.eupati.eu/patient-involvement/guidance-for-patient-involvement-in-industry-led-medicines-rd/> [Accessed May 17 2017]
- <sup>36</sup> European Patients Academy (EUPATI). Guidance Documents on Patient Involvement in R&D. Available from: <https://www.eupati.eu/guidance-patient-involvement/> [Accessed May 17 2017]
- <sup>37</sup> Patient Centered Outcomes Research Institute (PCORI). Financial Compensation Of Patients, Caregivers, And Patient/Caregiver Organizations Engaged In Pcori-Funded Research As Engaged Research Partners. Available from: <http://www.pcori.org/sites/default/files/PCORI-Compensation-Framework-for-Engaged-Research-Partners.pdf> [Accessed May 17 2017]
- <sup>38</sup> European Federation of Pharmaceutical Industries and Associations (EFPIA). EFPIA Code of Practice on Relationships Between the Pharmaceutical Industry and Patient Organizations (2011), Available from: [http://transparency.efpia.eu/uploads/Modules/Documents/code\\_po2011.pdf](http://transparency.efpia.eu/uploads/Modules/Documents/code_po2011.pdf) [Accessed May 17 2017]
- <sup>39</sup> International Committee of Medical Journal Editors (ICMJE). Available from: <http://www.icmje.org> [Accessed March 18 2016]
- <sup>40</sup> American Economics Association (2016). Available from: <https://www.aeaweb.org/>
- <sup>41</sup> Husereau, D., Drummond, M.F., Petrou, S., Carswell, C., Moher, D., Greenberg, D., et al. Consolidated health economic evaluation reporting standards (CHEERS) - explanation and elaboration: A report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. Value in Health, 2013;16(2):231-250.
- <sup>42</sup> Schulz K.F., Altman D.G., Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomized trials. Open Med 2010;4:e60–8
- <sup>43</sup> Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. Open Med 2009;3:e123–30
- <sup>44</sup> Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Guidelines for Economic Evaluation; Available from <https://www.equator-network.org/reporting-guidelines/cheers/> [Accessed May 17 2017]
- <sup>45</sup> STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) Statement. Available from: <http://www.strobe-statement.org/index.php?id=strobe-home> [Accessed May 17 2017]
- <sup>46</sup> Eddy et al. ISPOR-SMDM Modeling Task Force Report 7 on Model Transparency and Validity 2012
- <sup>47</sup> European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). The European Union electronic Register of Post-Authorisation Studies (EU PAS Register) Available from: [encepp.eu/encepp/studiesDatabase.jsp](http://encepp.eu/encepp/studiesDatabase.jsp) [Accessed May 17 2017]
- <sup>48</sup> International Committee of Medical Journal Editors (ICMJE). Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals (2016) Available from: <http://www.icmje.org/> [Accessed May 17 2017]
- <sup>49</sup> American Economics Association (2016). Available from: <https://www.aeaweb.org/>