1 THE COMPLEX INTERFACE BETWEEN ECONOMY AND HEALTHCARE:

2 AN INTRODUCTORY OVERVIEW FOR CLINICIANS

3

4 Federica Liliana Ottolini, M.D.[a]   federica_ottolini@libero.it

5 Laura Buggio, M.D.[a]   buggiolaura@gmail.com

6 Edgardo Somigliana, M.D.[b]   dadosomigliana@yahoo.it

7 Paolo Vercellini, M.D.[a,b]   paolo.vercellini@unimi.it

8

9 From [a]Department of Clinical Sciences and Community Health, Università degli Studi di Milano,

10 and [b]Fondazione Ca' Granda Ospedale Maggiore Policlinico

11 Via Commenda, 12 – 20122 Milano, Italy.

12

13 Corresponding Author: Paolo Vercellini, M.D.,

14 Istituto Ostetrico e Ginecologico 'Luigi Mangiagalli'- Università degli Studi di Milano,

15 Via Commenda, 12 - 20122 Milan, Italy.

16 Phone number: +39.02.5503.2917; e-mail: paolo.vercellini@unimi.it

17

20

21   ABBREVIATIONS:

22   EE, economic evaluation; OECD, Organization for Economic Co-operation and Development;

23   CEA, cost-effectiveness analysis; CER, cost-effectiveness ratio; ICER, incremental cost-

24   effectiveness ratio; WTP, willingness to pay; NICE, National Institute for Health and Clinical

25   Excellence; CUA, cost-utility analysis; QALY, quality adjusted life year; HUI, Health Utilities

26   Index; SF-6D, Short-form 6D; EQ-5D, Euro Quality of life 5 Dimensions.

27 ABSTRACT

28 In a period of generalized economic crisis, it seems particularly appropriate to try to manage a

29 continuing growing sector such as healthcare in the best possible way. The crucial aim of

30 optimization of available healthcare resources is obtaining the maximum possible benefit with the

31 minimum expenditure. This has important social implications, whether individual citizens or tax-

32 funded national health services eventually have to pay the bill. The keyword here is efficiency,

33 which means either, maximizing the benefit from a fixed sum of money, or minimizing the

34 resources required for a defined benefit. In order to achieve these objectives, economic evaluation is

35 a helpful tool. Five different types of economic evaluation exist in the health-care field: cost-

36 minimization, cost-benefit, cost-consequences, cost-effectiveness and cost-utility analysis. The

37 objective of this narrative review is to provide an overview of the principal methods used for

38 economic evaluation in healthcare. Economic evaluation represents a starting point for the

39 allocation of resources, the decision of the valuable investments and the division of budgets across

40 different health programs. Moreover, economic evaluation allows the comparison of different

41 procedures in terms of quality of life and life expectancy, bearing in mind that cost-effectiveness is

42 only one of multiple facets in the decision making-process. Economic evaluation is important to

43 critically evaluate clinical interventions and ensure that we are implementing the most cost-effective

44 management protocols. Clinicians are called to fulfill the complex task of optimizing the use of

45 resources, and, at the same time, improving the quality of healthcare assistance.

Introduction

Inadequacy of resources is the base of economy. For this reason, the need for optimization of the available resources appears of primary importance, with the objective of obtaining the maximum possible benefit with the minimum expenditure. [1]. In a context characterized by frequent cuts to public spending, the introduction in the health-care field of economic evaluations represents another intent of reconsidering a sector that consumed 8.8% of Italian gross domestic product (GDP) in 2013, excluding capital expenditure, compared with an OECD (Organization for Economic Co-operation and Development) average of 8.9% [2]. As a reflection of the economic crisis, health spending continued to shrink in Greece, Italy and Portugal in 2013 [3]. On the contrary, in the last five years health spending has been growing with a medium rate of 2.5% per year outside Europe [3].

As a consequence, it seems appropriate to try to obtain the best allocation of the finite available resources at our disposal, in order to guarantee health assistance despite the negative effects of the economic crisis and to manage in the proper way a continuing growing sector. The keyword here is *efficiency*, which means either maximizing the benefit from a fixed sum of money or minimizing the resources required for a defined benefit [1]. This has important social implications, whether individual citizens or tax-funded national health services eventually have to pay the bill. Considering that the healthcare budgets are limited and spending in one area is unavoidably at the expense of investment in another, efficiency can be interpreted as ensuring that the benefits obtained exceed the benefits forgone [1]. The latter concept could be also express as "opportunity cost" [4].

The objective of this narrative review is to appraise the most recent evidence regarding economic evaluation and healthcare spending. In fact, the priority is to try to disseminate information and implement this model within the health community, with the aim of handling appropriately the financial resources, ensuring the wellbeing of the patient at the first place.

Methods

For this review, the best quality evidence was selected with preference given to the most recent and definitive original articles and reviews. Information was identified by searches of MEDLINE and references from relevant articles, using combinations of MESH terms "economic evaluation", "cost-effectiveness analysis", "cost-effectiveness threshold" "cost-utility analysis", "efficiency", "health economic evaluation", "health care economic analyses", "value based medicine", "NICE" "utility" and "QALY". The search was limited to peer-reviewed, full-text articles in the English language. For most issues, papers published between January 2003 and December 2015 were considered.

Two authors (FLO and LB) performed an initial screening of the title and abstract to exclude citations deemed inappropriate for the present narrative review (e.g., experimental studies or investigational health economic analyses relative to specific treatments). Articles describing the various approaches with an apparent didactic format were retrieved and assessed. A total of 22 articles that were deemed more informative and clear by both reviewers were eventually selected and analyzed in detail (1, 2; 5-24). No formal system was adopted to rate the quality of the evaluated articles. Four reviews (16-19), written by an ophthalmology research group, were excluded because they were analogous to a fourth included article (15). For a similar reason, we excluded one review (20) and included another one (1) previously published by the same author. Two articles (21, 22) were excluded as they explained how to conduct a specific economic analysis, rather then describe the general characteristics of the various methods. One article (23) was excluded because it focused on methodological and interpretative aspects of economic analysis. One article (24) was excluded as only cost-utility and cost-benefit analysis were addressed, but not cost-effectiveness analysis. A total of 13 articles were eventually included in the present review.

Types of economic evaluation

In the most commonly used economic evaluations, two interventions, a standard treatment and an experimental one are compared with the scope of assessing the value of the novel procedure. When

98   the latter is more cost-effective than the older one, the novel procedure is obviously chosen; on the

99   other hand, if the new treatment is more expensive and less effective, the standard one is generally

100   maintained. Uncertainty arises when the novel treatment is more effective but also more expensive

101   than the traditional treatment [5]. The scenario becomes more complex when evaluations aim at a

102   more comprehensive approach, i.e. the comparison between interventions of highly distinct medical

103   areas.

104   Five different types of economic evaluations exist in the health-care field: cost-

105   minimization, cost-benefit, cost-consequences, cost-effectiveness and cost-utility analysis [5]

106   (Table 1):

107   - *Cost-minimization analysis:* in cost-minimization analysis, two or more interventions with

108   equivalent consequences in terms of benefit are compared [1]. It should ideally be used only when

109   comparing treatment of equal effectiveness, and it focuses on costs alone to help choosing the

110   cheapest option [6].

111   - *Cost-benefit analysis:* it evaluates, in monetary terms, cost and consequences of an intervention

112   [1]; if the monetary value of an intervention exceeds the cost of the intervention, then the

113   intervention is acceptable. [7]. This analysis places money values on both inputs (costs) and outputs

114   (general benefits) of health care and represents the best method to inform allocation decisions

115   because it consents to compare interventions from highly heterogeneous areas and it is based on a

116   more comprehensive economic vision of the society [4].

117   - *Cost-consequences analysis*: this analysis reflects how decisions are made in the real world. This

118   approach is often used when various outcomes cannot be condensed into a single measure that

119   summarizes benefits and costs. For example, in a cost-consequences analysis, the general

120   practitioner and nurse's salaries as well as expenditures sustained by patients are considered as

121   costs, whereas patient health state and satisfaction with treatment are considered as consequences

122   [1].

123   - *Cost-effectiveness analysis (CEA)*: it is the most widely used analysis and it consents to compare

124   interventions with a common health outcome. The outcomes could be measured using different

125   ratios (for example, cost per life year gained or pain free days) [1]. This data should be obtained,

126   when possible, from clinical trials [8]. CEAs provide a definite answer on a specific comparison,

127   i.e. it concludes which of the compared options has a more favorable cost-effectiveness profile.

128   However, a less cost-effectiveness procedure may still be of economic and clinical interest if it is

129   more effective. To disentangle this possibility, one may rely on the incremental cost effectiveness

130   ratio (ICER). Specifically, the cost effectiveness ratio (CER) expresses the ratio between the cost of

131   an intervention (K) and the benefit endpoint gained (E). The ratio K/E describes a treatment's

132   marginal costs per gained clinical benefit unit [9]. The ICER allows the comparison between

133   different interventions for the same pathology. Considering respectively K_1 and K_2 as the costs of

134   the standard treatment and the novel one, and E_1 and E_2 as the benefit endpoints of the two

135   interventions, the ICER is calculated as [9]: ICER= $(K_2-K_1) / (E_2-E_1)$. This ratio permits to define

136   the additional costs for unit of benefit gained with the new treatment with the possibility of drawing

137   a "health economical ranking" of the different procedures [9].

138   Before comparing the ICERs, it's fundamental to estimate the cost-effectiveness benchmark,

139   which expresses the insurer's maximum willingness to pay (WTP) additional treatment costs per

140   gained benefit unit. The new treatment will be selected only if the ICER is inferior of the

141   benchmark [9].

142   The objective is to establish the socially acceptable CER. As Noyes and Holloway [10]

143   stated: "Is the additional effects of our new technology compared with the old technology worth the

144   additional costs?". The most suitable cost-effectiveness benchmark to be used should be adapted to

145   the local economical situation but remains highly debated. In the affluent Western world, the

146   thresholds used are generally more or less equivalent to the gross domestic product (GDP) pro

147   capita [11]. The National Institute for Health and Clinical Excellence (NICE) has established a cost-

148   effectiveness threshold range between £ 20.000 and £ 30.000 per life year gained.[11] However,

149 this kind of analysis could be performed only if the compared interventions use a common unit of

150 effectiveness, such as cost per life year gained [8]. In addition, a cost-effectiveness analysis might

151 examine this intervention in terms of quantity and not of quality [8].

152 - *Cost-utility analysis (CUA):* represents an economic evaluation that aims at defining the patient's

153 preference for being in a particular health-state [4]. In CUA all the outcomes analyzed are expressed

154 in terms of QALY (quality adjusted life year). With this method it is possible to compare treatments

155 used in different stages of a pathology and "opportunity cost" could be measured [4]. It consents to

156 compare interventions from very different medical disciplines or interventional areas, such as, for

157 instance a vaccine program and an ambulance referral system. CUAs thus represent a valuable

158 instrument for taking decisions regarding the allocation of public health resources.

159 Contrary to CEA, which analyses a benefit of an intervention only in terms of quantity,

160 CUA focuses also on quality and include also the preferences of the patient [8]. The effectiveness of

161 an intervention is measured through its utility value [8] that is ranged between 0 (worst health) and

162 1 (best health). Then, by multiplying the utility value with the length of time in that state, QALYs

163 are obtained [8]. Several direct methods exist to calculate the utility value. These include scaling

164 methods, such as visual analogue system, and choice methods such as the time trade-off and

165 standard gamble [7].

166 The visual analogue system is a linear scale that runs from 0 to 1, 10 or 100, with the higher

167 values representing the perfect health and 0 the worst health state conceivable (or death) [7].

168 Strengths of this method include the easiness of use and the possibility of answering by postal

169 survey. Moreover, the visual analogue system requires no "trade-off" or choice and the individual

170 does not have to justify his preference based on monetary, time or health factors [7].

171 In the standard gamble, the individual chooses between remaining in the actual state of

172 chronic health for the rest of his life or picking an uncertain gamble: the possibilities are of being

173 healthy for the rest of their life, with a probability of *p,* or immediate death, with a probability of 1-

174 *p* [10]. The amount of *p* range from 1.0 to 0.1 until a point of indifference is reached, which defines

175   the utility weighting [7]. Advantages of standard gamble are the combination of time, risk and

176   quality. At the same time these characteristics could represent a weakness, in particular in those

177   individuals who are time-sensitive and are not prone in taking risky decisions [7].

178   The time trade-off system is the method most frequently adopted in the calculation of

179   QALYs. The individual has to make a choice between two different options: a diminished health

180   state for a definite time or a full heath state for a shorter life span [7]. Choosing the second

181   alternative means the sacrifice of a period of life span in exchange of a shorter period of full health

182   state. For example, if the patient has a life expectancy of 30 years with a specific pathological

183   condition and decides to reduce it to 15 years with a full health status, the value of his actual health

184   state is 15/30, i.e. 0.5. This system involves a choice and balances both quality and quantity.

185   Limitations include the reluctance of exchanging time for health due to personal, philosophical or

186   religious beliefs [7].

187   Moreover, the utility value could be measured with indirect methods like questionnaires,

188   such as Health Utilities Index (HUI), Short-form 6D (SF-6D), and Euro Quality of life 5

189   Dimensions (EQ-5D) [4].

190   Specific fields that require a CUA include the importance of quality of life as effectiveness

191   outcome, when the intervention has an impact on both morbidity and mortality, when the

192   intervention have a multiple range of different outcomes with the aim of producing a single general

193   outcome for comparison, and when resources must be allocated from a fixed budget [4]. The main

194   drawback of CUA is the use of measures (QALYs) obtained from population samples, which reflect

195   the mean value of the general population, that, at the same time, could differ from the specific

196   interests of the single individual [12].

197

198   **Discussion**

199   Key points correlated with the interpretation of the results of an economic evaluation include the

200   perspective and time horizon, from which the lost and gained costs can be estimate [10]. It should

201 be underlined that multiple kinds of perspectives exist: "personal", "health insurance", "provider"

202 and "societal". The societal perspective takes account of all costs, and is the most suitable one.

203 Moreover, the societal perspective considers not only the individual patient's costs but also the

204 disbursement of the insurance and the National Health System, obtaining a global analysis [10].

205 At the same way, the temporal definition of the time horizon, considering that same benefit could

206 require several years to manifest, appears of fundamental importance [10].

207   Another aspect to consider is the possible creation of an inter-individual conflict of values.

208 In fact, we have to take into account the impact of individual preferences even when general

209 population preferences are used to value the benefits of interventions [12]. Furthermore, patient's

210 preferences have a rebound on efficacy outcomes, partly due to the inadequate compliance of the

211 patient to therapy, and to personal psychological factors [12].

212   In clinical practice the patient alone is assumed to make the definitive treatment choice, after

213 receiving all the technical information from the clinician. The figure of the clinician is located in the

214 middle of this "conflict", trying to reach a balance between the ideal treatment and the healthcare

215 budget [12]. In order to overcome this situation, it could be advisable to adopt a two-part decision

216 process [12]: the detection of the most cost-effective therapy according to mean population values,

217 and the identification of those treatments that are cheaper than the most cost-effective therapy.

218   In the individual patient-doctor relationship, the clinician should describe in detail all the

219 potential benefits and harms of the available therapeutic alternatives. Fully informed patients are

220 more likely to choose treatments that show a net benefit [25]. In this regard, the inclusion of the

221 extra cost for the net benefit of different treatments is fundamental in health care economic

222 evaluation.

223   However, when prescribing a treatment or a procedure, doctors carry a responsibility also

224 for future patients and for the society at large, especially within a tax-funded national health system.

225 In fact, when a fixed budget is managed, the use of resources for a category of patients is

226 unavoidably at the expense of another one. This is known as "opportunity cost".

227 The main objective of any cost evaluation approach is the optimization of the use of finite

228 resources. Economic evaluation allows a transparent and logical use of a predetermined budget

229 according to an equity value. In fact, patients have different health conditions that require different

230 expenditure of resources but, eventually, the result in terms of overall health benefit should be

231 similar for all patient categories.

232 In order to achieve the above objectives, physicians should foster high-value interventions

233 [26]. The introduction of the concept of value-based medicine in the health service daily practice

234 appears of fundamental importance also from the economic perspective. Value-based medicine is

235 obtained by matching the value of an intervention, in terms of QALYs, to evidence-based medicine.

236 Healthcare providers should not only demonstrate the efficacy of a procedure, but also analyze its

237 impact on quality of life and on financial resources. The final target of value-based medicine is

238 maximizing the use of resources, and, at the same time, improving the quality of the healthcare

239 assistance [15].

240 Value is a word that arouses skepticism, because it is often misunderstood and conceived as

241 cost reduction [27]. Conversely, value-based medicine could represent the highest form of

242 efficiency and social equity that health care providers and medical decision-makers could offer to

243 individual patient and society as a whole, as it constitutes a balance between potential benefits,

244 potential harms and cost of care, and takes into account patient priorities and preferences [28]. The

245 medical educational training itself should be restructured with the objective of de-adopting low-

246 value care. According to Schwartz, "medical students; interns; residents; and fellows must learn

247 that their mentors and teachers are judging them not only by their ability to properly perform a

248 procedure but also by their having the expertise in clinical decision making to know when and why

249 that procedure is medically appropriate" [29].

250 An additional point to stress is the amount of money that the government is prone to pay to

251 gain an extra unit of benefit. As previously stated in the United Kingdom, the NICE has established

252 a cost-effectiveness threshold range between £20.000 and £30.000 with the aim of obtaining an

253 optimal allocation of limited resources [11]. This threshold should be periodically reassessed to

254 guarantee that it captures the impact of modifications in efficiency and budget over time [11].

255 Maynard and Bloor [13] emphasize the bipolar role of the UK government, as both regulator and

256 sponsor of the pharmaceutical industry. NICE approves only treatments that have shown to produce

257 a QALY for an adequate cost, and commissioners are obliged to fund it. In order to obtain a

258 reimbursement, pharmaceutical industries need to comply with a cost-QALY ratio inferior to

259 £30.000 [13]. In recent years, pharmaceutical industries have lobbied NICE for the widening of the

260 cut-off for reimbursement, especially for cancer treatments, that are particular expensive. The risk is

261 the creation of an unequal logic, in which the cost-effectiveness of a specific treatment is placed in

262 second line [13]. Moreover, this choice of reimburse only cancer treatments, which cost exceed the

263 threshold of £30.000, discriminates against other disease which may be equally in need of

264 additional funding [13].

265 The economic evaluation represents a starting point for the allocation of the resources, the

266 decision of the valuable investments, and the division of the budget across different health

267 programs. Moreover, economic evaluations allow the comparison of different procedures in terms

268 of quality of life and life expectancy, remembering that cost-effectiveness is only one of multiple

269 facets in the decision-making process. On the other hand, economic evaluations are seen as an

270 insensible form of utilitarianism and mistrust due to the idea of a "rationing" of the health care

271 resources. In reality, economic evaluations consent a rational and methodical partition of resources,

272 in a process of transparency in the decision-making context [14].

273

274 **Learning points**

275 • Particularly in a period of economic crisis, maximizing the available health care resources in

276 order to appropriately manage pre-determined financial budgets, and obtaining the greatest

277 benefit with the minimum expenditure, according to efficiency, is essential.

278 • Economic evaluation is the starting point for allocation of finite health care resources.

279   • There are five different types of economic evaluation: cost-minimization analysis, cost-

280   benefit analysis, cost-consequences analysis, cost-effectiveness analysis, cost-utility

281   analysis.

282   • The main analysis is cost-utility, and the measure is cost per QALY; it focuses on patient's

283   preferences and on quality of life.

284   • In economic evaluation analysis it is crucial to consider different perspectives, i.e., time

285   horizon, patient compliance, and the extra amount of money that healthcare administrators

286   are prone to pay with the aim of obtaining the extra benefits.

287   • The next frontier is value-based medicine, achieved by matching the value of an intervention

288   with the evidence-based medicine.

289   • The end-result of economic evaluation in health care is not rationalization of resources but

290   social equity, that is, providing the best possible medical care to as many as possible people.

291

292 **Conclusion**

293 Physicians represent a key figure in the management of resources for the wellbeing of patients, and

294 they must learn how to allocate in the best possible way the finite budget they have. Therefore, the

295 role of the physician and the ability in communicating with the patient are of utmost importance. In

296 fact, the gold standard intervention (on the basis of economic evaluation) may not coincide with the

297 one chosen by the patient, and the patient's compliance has a rebound on the effectiveness of the

298 treatment [12].

299   Contrary to common belief, careful administration of resources does not mean

300 transformation of physicians in economic managers more focused on budgets than on patient health.

301 Conversely, the combination of available evidence and economic analysis into value-based

302 medicine represents optimization of the efficiency of the system, supporting the use of a transparent

303 decision process. The physician has to select the best intervention in terms of efficacy and

304 effectiveness, using a different amount of resources from patient to patient, tailoring a specific

305 treatment for individual cases, respecting at the same time the principles of patient-centered

306 medicine and equity [26].

307   In spite of the innumerable economic evaluations conducted in recent years, the cornerstones

308 of these evaluations are rarely performed in clinical practice [14]. The conduction of randomized

309 controlled trials aimed at assessing the impact of various economic evaluations, could constitute

310 another step forward in order to draft specific guidelines providing economic indications for

311 medical choices.

312   Economic evaluation in health-care is important to critically assess medical interventions

313 and guarantee the most cost-effective management protocols [4]. The goal of such an approach is

314 not to do less or "rationalize" the expenditure, but to allow qualitative improvements in clinical

315 practice and to offer an equal assistance to as many citizens as possible.

316

322

325

326 **References**

327 [1] Kernick DP. Introduction to health economics for the medical practitioner. Postgrad Med J

328 2003;79:147-50.

329 [2] OECD Health Statistics 2015 - Country Notes. http://www.oecd.org/els/health-systems/Country-

330 Note-ITALY-OECD-Health-Statistics-2015.pdf [last visit 05/01/2016].

331 [3] OECD Health Statistics 2015. http://www.oecd.org/els/health-systems/health-expenditure.htm. .

332 [last visit 23/12/2015].

333 [4] Rudmik L, Drummond M. Health economic evaluation: important principles and methodology.

334 Laryngoscope 2013;123:1341-7.

335 [5] Zilberberg MD, Shorr AF. Understanding cost-effectiveness. Clin Microbiol Infect

336 2010;16:1707-12.

337 [6] Vernazza C, Heasman P, Gaunt F, Pennington M. How to measure the cost-effectiveness of

338 periodontal treatments. Periodontol 2000 2012;60:138-46.

339 [7] Hamilton D, Hulme C, Flood L, Powell S. Cost-utility analysis and otolaryngology. J Laryngol

340 Otol 2014;128:112-8.

341 [8] McFarland A. Economic evaluation of interventions in health care. Nurs Stand 2014; 29:49-58.

342 [9] Krummenauer F, Landwehr I. Incremental cost effectiveness evaluation in clinical research. Eur

343 J Med Res 2005;10:18-22.

344 [10] Noyes K, Holloway RG. Evidence from cost-effectiveness research. NeuroRx 2004;1:348-55.

345 [11] McCabe C, Claxton K, Culyer AJ. The NICE cost effectiveness threshold: what it is and what

346 that means. Pharmacoeconomics 2008;26:733-44.

347 [12] Brazier JE, Dixon S, Ratcliffe J. The role of patient preferences in cost-effectiveness analysis:

348 a conflict of values? Pharmacoeconomics 2009;27:705-12.

349 [13] Maynard A, Bloor K. Regulation of the pharmaceutical industry: promoting health or

350 protecting wealth? J R Soc Med 2015;108:220-2.

351 [14] Douglas HR, Normand C. Economic evaluation: what does a nurse manager need to know? J

352 Nurs Manag 2005;13:419-27.

353 [15] Brown GC, Brown MM, Sharma S. Value-based medicine: evidence-based medicine and

354 beyond. Ocul Immunol Inflamm 2003;11:157-70.

355 [16] Brown MM. Health care economic analyses. Curr Opin Ophthalmol 2003;14:117-21.

356 [17] Busbee BG, Brown GC, Brown MM. Cost-effectiveness of ocular interventions. Curr Opin

357 Ophthalmol 2003;14:132-8.

358 [18] Brown MM, Brown GC, Sharma S, Landy J. Health care economic analyses and value-based

359 medicine. Surv Ophthalmol 2003;48:204-23.

360 [19] Brown GC, Brown MM, Sharma S. Health care economic analyses. Retina 2004;24:139-46.

361 [20] Kernick D. An introduction to the basic principles of health economics for those involved in

362 the development and delivery of headache care. Cephalalgia 2005;25:709-14.

363 [21] Mitton C, Jarrell JF. Economic evaluation in obstetrics and gynaecology: principles and

364 practice. J Obstet Gynaecol Can 2003;25:219-23.

365 [22] Virgili G, Koleva D, Garattini L, Banzi R, Gensini GF. Utilities and QALYs in health

366 economic evaluations: glossary and introduction. Intern Emerg Med 2010;5:349-52.

367 [23] Higgins AM, Harris AH. Health economic methods: cost-minization, cost-effectiveness, cost-

368 utility, and cost-benefit evaluations. Crit Care Clin 2012;28:11-24.

369   [24] Moayyedi P, Mason J. Cost-utility and cost-benefit analyses: how did we get there and where

370   are we going? Eur J Gastroenterol Hepatol 2004;16:527-34.

371   [25] Lin GA, Redberg RF. Addressing Overuse of Medical Services One Decision at a Time.

372   JAMA Intern Med 2015;175:1092-3.

373   [26] Vercellini P, Giudice LC, Evers JL, Abrao MS. Reducing low-value care in endometriosis

374   between limited evidence and unresolved issues: a proposal. Hum Reprod 2015;30:1996-04.

375   [27] Lee TH. Putting the value framework to work. N Engl J Med 2010;363:2481-3.

376   [28] Colla CH. Swimming against the current -- what might work to reduce low-value care? N Engl

377   J Med 2014;371:1280-3.

378   [29] Schwartz FH. The challenge of deadopting low-value care. Ann Intern Med 2014;161:842-3.

379   [30] Kim RD, Kapur VK, Redline-Bruch J, Rueschman M, Auckley DH, Benca RM et al. An

380   Economic Evaluation of Home versus Laboratory-Based Diagnosis of Obstructive Sleep Apnea.

381   Sleep 2015;38:1027-37.

382   [31] Tompa E, Dolinschi R, Alamgir H, Sarnocinska-Hart A, Guzman J. A cost-benefit analysis of

383   peer coaching for overhead lift use in the long-term care sector in Canada. Occup Environ Med

384   2016;73:308-14.

385   [32] Al Shakarchi J, Inston N, Jones RG, Maclaine G, Hollinworth D. Cost analysis of the

386   Hemodialysis Reliable Outflow (HeRO) Graft compared to the tunneled dialysis catheter. J Vasc

387   Surg 2016;63:1026-33.

388   [33] Bernard-Arnoux F, Lamure M, Ducray F, Aulagner G, Honnorat J, Armoiry X. The cost-

389   effectiveness of tumor-treating fields therapy in patients with newly diagnosed glioblastoma. Neuro

390   Oncol 2016;0:1-8.

391   [34] Murphy A, McCarthy FP, McElroy B, Khashan AS, Spillane N, Marchocki Z et al. Day

392   care versus inpatient management of nausea and vomiting of pregnancy: cost utility analysis of a

393   randomised controlled trial. Eur J Obstet Gynecol Reprod Biol 2016;197:78-82.

Types of economic evaluation	Measure	Advantages	Disadvantages	Examples of clinical studies
Cost-minimization analysis	Difference in monetary terms between interventions	Easiness of execution	Focused on costs only	**An Economic Evaluation of Home Versus Laboratory-Based Diagnosis of Obstructive Sleep Apnea [30]** In a RCT, given that 3-month clinical outcomes were equivalent, the cost of home-based diagnosis of obstructive sleep apnea was $264 less for the payer (95% CI $39, $496) compared with laboratory-based diagnosis, whereas a difference of $40 (95% CI, $213 - $142,) in favor of the laboratory arm diagnosis was observed from the provider perspective.
Cost-benefit analysis	Net gain or loss in monetary terms	Same measure for benefit and costs	Limited applicability, not always possible to measure benefit in monetary terms (e.g., lives saved)	**A cost-benefit analysis of peer coaching for overhead lift use in the long-term care sector in Canada [31]** A peer-coaching program for patient ceiling lift use was associated with a reduction in the patient-handling injury rate of 34% during the program and 56% after the program concluded, with an estimated 62 lost-time injury claims averted, with a modest monetary cost. The monetary benefits and costs to the system were, respectively, $748431 and 894000, with a benefit-to-cost ratio of 0.84.
Cost-	Various outcomes	Reflects the complexity	Decision-making is	**Cost analysis of the Hemodialysis Reliable**

consequences analysis	(not a single measure)	of the real world	difficult because there is not a single measure to compare interventions	**Outflow (HeRO) Graft compared to the tunneled dialysis catheter [32]** A 100-patient cohort managed with the HeRO Graft experienced 6 fewer failed devices, 53 fewer access-related infections, and 67 fewer device thrombosis compared to patients managed with tunneled dialysis catheter (TDCs). Although the initial device and placement costs for the HeRO Graft are greater than those for TDCs, savings from the lower incidence of device complications and longer effective device patency reduces these costs. Overall net annual costs are £2600 for each HeRO Graft-managed patient compared to TCD-managed patients. If the U.K. National Health Service were to reimburse hemodialysis at a uniform rate regardless of the type of vascular access, net 1-year savings of £1200 per patient are estimated for individuals managed with the HeRO Graft.
Cost-effectiveness analysis	Cost-effectiveness ratio (CER) or incremental cost effectiveness ratio (ICER)	Measures the additional cost per unit of benefit and allows drawing a "health economical ranking" of different procedures	Applicable only if the compared interventions use a common health outcome (unit of effectiveness)	**The cost-effectiveness of tumor-treating fields therapy in patient with newly diagnosed glioblastoma [34]** Tumor-treating fields (TTF) therapy consists of a medical device that creates low-intensity and intermediate-frequency electric fields with an antimitotic effect on glioblastoma cells. According to the preliminary results of a RCT, the addition of TTF therapy to the standard protocol

			Analyses the interventions in terms of quantity and not of quality of life.	(radiotherapy combined with temozolomide) for newly diagnosed patients with glioblastoma resulted in a life expectancy of 22.08 months compared with 18 months after the conventional therapy strategy. The incremental effectiveness, expressed as life-years gained, was 4.08 months in favor of TTF strategy. The total costs, from a provider's perspective, were €243 141 for TTF and €57 665 for the standard therapy strategy. The incremental cost-effectiveness (ICER) was thus €549 909 per life-year gained (see text for the formula).
Cost-utility analysis	Cost-utility ratio (cost per QALY[a], quality adjusted life years),	Focuses on patient's preference for being in a particular state of health

Allows comparison between different treatments used in various stages of a disease with different unit of benefit

Analyses the interventions in terms of both quality and quantity of life | QALYs reflect the mean value of the general population, which might differ from the specific priorities of the individual patient | **Day care versus inpatient management of nausea and vomiting of pregnancy: cost utility analysis of a randomized controlled trial [34]**

Data were obtained from a recently published RTC to asses the cost-effectiveness of day care versus inpatient management of nausea and vomiting of pregnancy (NVP). Costs and outcomes were considered with the perspective of the health care provider and patients. The primary study outcome was the total number of inpatient nights related to nausea and vomiting. The median number of inpatient admissions were fewer for day care compared to inpatient management. The mean cost was €985 per patient in day care management, and €3837 per patient in inpatient management, considering both the health system and the patients' perspectives. Thus, day care management is less costly. The QALYs estimated for day care and inpatient |

| | | Represents the best method to allocate resources from a fixed budget | | management were, respectively, 9.49 and 9.42. Thus, day care management is more cost effective. The cost-utility ratio (the cost of a treatment divided for QALYs generated from that treatment) for day care management is €985 /9.49= €103.79 per QALY, whereas for inpatient management is €3837/9.42= €407.32 per QALY. |

Table 1. Characteristics of different methods for economic evaluation in health care.

[a] QALY= utility value (from 0 to 1) multiplied with the length of time in that state