

1 *Review*

2 **Inhospital Palliative Care: Should We Need to Reconsider** 3 **What Role Hospitals Should Have in Patients with End-Stage** 4 **Disease or Advanced Cancer?**

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13 **Abstract:** Traditionally, palliative care (PC) systems focused on the needs of advanced cancer
14 patients. But, most patients needing PC have end-stage organ diseases. Similarly, PC models
15 focused on the needs of patients in hospice or at home; however, in most cases PC is provided in
16 acute hospitals. Indeed, the symptom burden that these patients experience in the last year of life
17 frequently forces them to seek care in Emergency Department. The majority of them are admitted to
18 the hospital and many die. This issue poses important concerns. Despite the efforts of attending
19 healthcare professionals, inhospital patients do not receive optimal care near the end-of-life. Also,
20 evidence is emerging that delay in identifying patients needing PC have a detrimental impact on
21 their quality of life (QoL). Therefore, there is an urgent need to early and properly identify these
22 patients among those hospitalized. Several trials reported the efficacy of PC in improving the QoL
23 in these patients. Each hospital should ensure that a multidisciplinary PC team is available to
24 support attending physicians to achieve the best QoL for both PC patients and their families. This

25 review discusses the role and the impact of inhospital PC in patients with end-stage disease or
26 advanced cancer.

27

28 **Keywords:** palliative care team, seriously ill patients, end-of-life, quality of life, symptom relief,
29 acute palliative care unit, cost savings

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33 **1. Palliative care: for who?**

34 The World Health Organization defines palliative care as: “is an approach that improves the
35 quality of life of patients and their families facing the problem associated with life-threatening
36 illness, through the prevention and relief of suffering by means of early identification and
37 impeccable assessment and treatment of pain and other problems, physical, psychosocial and
38 spiritual” [1].

39 Aging of the population as well as advances in medicine and public health is currently
40 increasing the prevalence of people affected by progressive, chronic, life-limiting illnesses who
41 would benefit of a palliative care (PC) approach. This phenomenon represents a great challenge for
42 the healthcare systems especially in terms of patients’ assistance and healthcare costs [2].

43 Traditionally, PC services have been focused on the needs of cancer patients with advanced or
44 metastatic disease. As a matter of fact, inhospital PC programs have also begun to pay attention on
45 the needs of patients affected by non-oncological diseases, such as end-stage organ failures (heart
46 failure, chronic obstructive pulmonary disease –COPD–, liver cirrhosis, and severe renal
47 dysfunction), as well as neurological illnesses (amyotrophic lateral sclerosis, Parkinson’s disease,
48 multiple sclerosis, Alzheimer’s, and other dementias) [3,4]. Actually, it is important to underline
49 that patients with cancer or heart, chronic obstructive pulmonary, and renal diseases at an advanced
50 stage have been demonstrated to share a similar spectrum of symptoms, and have a common

51 pathway during the last period of their illness trajectories [5]. Therefore nowadays, the area of
52 action of PC is the relief of symptoms as well as psychological, social, and spiritual issues of
53 patients with chronic life-limiting diseases, regardless of the diagnosis [3].

54

55 **2. Why do patients with chronic serious illness visit the emergency department near the end of** 56 **life?**

57 During the last 6-12 months of life, most of the patients with end-stage disease or advanced
58 cancer experience an increase in symptom burden which forces them to seek care in acute hospital.
59 These patients are usually admitted to the Emergency Department (ED) in order to administer them
60 urgent care for the relief of uncontrolled symptoms [6]. Frequently, the visit may be precipitated by
61 the distress of family members near the end of life (EoL) [7].

62 A recent study, which has focused on the PC symptom management, has identified pain,
63 dyspnea, nausea and vomiting, anorexia, anxiety, and constipation as the most frequent symptoms
64 in seriously ill patients who are admitted to the ED, regardless of the specific disease. In addition,
65 dehydration and acute urinary retention are other common symptoms of these patients when they
66 come to an ED [8].

67 Nearly 50% of patients experience uncontrolled pain at the EoL [5]. Worsening dyspnea is
68 also frequent in patients in need of PC. Diseases commonly causing severe dyspnea are acute
69 exacerbations of COPD, lung cancer, and congestive heart failure. Frequent causes of increased
70 shortness of breath are pneumonia, pulmonary embolism, pleural effusion, pericardial tamponade,
71 pneumothorax, and superior vena cava syndrome. Nausea and vomiting are common
72 gastrointestinal symptoms in these patients due to several causes: medications (opioids,
73 chemotherapy agents), bowel obstruction, impaired gastric emptying, constipation, and increased
74 intracranial pressure. Frequently, reduced oral food intake or severe weight loss due to anorexia
75 (appetite loss), dysphagia, early satiety, stomatitis, and taste changes are common reasons for visits
76 to the ED. Anxiety, confusion or delirium in seriously ill patients represent a quite frequent cause of

77 access to the ED, as its management in home setting can be very difficult. Constipation is found in
78 up to 90% of PC patients, regardless of the underlying illness. Constipation is typically caused by
79 opioid intake, but also by bowel obstruction in patients bearing peritoneal carcinomatosis or
80 advanced intra-abdominal tumors.

81 Sometimes, patients with end-stage disease or advanced cancer need in the ED of procedures
82 such as intravenous fluids infusion for dehydration, placement of a urinary catheter for acute
83 urinary retention, paracentesis for symptomatic intractable ascites or thoracentesis for symptomatic
84 severe pleural effusion.

85

86 **3. How to identify patients in need of palliative care?**

87 Unfortunately, in the medical literature there is no agreement about the definition of the
88 ‘palliative care patient’ [9]. Evidence is emerging that delay or lack in identifying patients in need
89 of PC have a potential harmful impact on their care [10]. In fact, a delayed recognition of those
90 patients is associated with inadequate continuity of care, insufficient support, and increased
91 healthcare costs [11]. Therefore, there is an urgent need to early and properly identify among
92 hospitalized seriously ill patients those in need of PC.

93 The ED should be considered as a critical point of PC access for patients with end-stage
94 disease or advanced cancer [12,13]. In our study, we found that more than one-third of people
95 affected by these chronic diseases awaiting to be hospitalized after an ED visit should be identified
96 as in need of PC consultation [14]. In order to identify the patients in need of PC, we took into
97 account for cancer patients the indicators elaborated by the National Comprehensive Cancer
98 Network (NCCN) [15] and for patients with end-stage diseases the criteria proposed by the Italian
99 Society of Anesthesia Analgesia Resuscitation and Intensive Care (SIAARTI) [16]. This study
100 demonstrated the feasibility of applying NCCN/SIAARTI screening tools to identify patients in the
101 ED for referral to a PC team.

102 The identification of PC needs in the ED, at the beginning of the hospital course, might
103 provide a greater benefit to patients, families, and hospitals to anticipate PC consultation, which
104 often occurs later in a patient's hospital course. Wu *et al.* showed that PC consultation in the ED
105 was associated with a significantly shorter length of stay for the patients admitted to the hospital
106 [17]. Grudzen *et al.* demonstrated that an ED-initiated PC consultation improved quality of life
107 (QoL) without shortening survival in advanced cancer patients [18].

108

109 **4. What role for in-hospital palliative care?**

110 Historically, PC models focused on the needs of patients in hospice or at home. However,
111 many patients with end-stage disease or advanced cancer experience repeated unplanned hospital
112 admissions, particularly in the last year of life [19]. In our study, we observed that about 75% of the
113 patients affected by these diseases in need of PC, awaiting hospitalization after admission to the
114 ED, had more than one in-hospital admission during the last year [14]. Moreover, in high-income
115 countries the majority of patients with end-stage disease or advanced cancer die in the hospitals [20]
116 and this issue poses important concerns.

117 In 1995, the first large controlled trial investigating the EoL decision-making in seriously ill
118 hospitalized patients was published [21]. The aim of this Study was to Understand Prognoses and
119 Preferences for Outcomes and Risks of Treatments (SUPPORT trial) in 9105 adults hospitalized
120 patients with life-threatening diagnoses. The five analyzed outcomes were: 1) pain; 2) days in an
121 intensive care unit (ICU), comatose or receiving mechanical ventilation before death; 3) hospital
122 resource use; 4) incidence and timing of written do-not-resuscitate (DNR) orders; and 5) patient-
123 physician agreement on cardiopulmonary resuscitation preferences. The authors concluded that the
124 care of seriously ill or dying hospitalized patients was not attractive.

125 Care of patients with chronic life-limiting illnesses has been recognized in the recent years as
126 suboptimal in hospital settings [22-25]. Particularly, patients and their families often complain

127 inadequate relief of pain and other symptoms as well as futile diagnostic imaging and unwanted
128 life-sustaining treatments at the EoL [26-28].

129 Another unmet need is the communication between attending physicians and
130 patients/relatives. Frequently this communication is inadequate in explaining complex medical
131 information including prognosis and treatment options, resulting in misunderstandings mainly at the
132 EoL [29,30]. Moreover, referral to hospice are implemented late in the course of illness by
133 physicians, despite was observed that family members of persons referred too late reported lower
134 satisfaction with hospice services [31,32].

135 Muir and Arnold reported that often dying patients in acute care hospitals were in physical
136 pain, without attention to the emotional and spiritual suffering [33]. The authors emphasized that
137 hospital physicians should become the primary providers of PC for these hospitalized patients with
138 end-stage diseases.

139 The weak point of this model is that the majority of hospital healthcare professionals do not
140 currently receive proper teaching on communication, especially concerning EoL care in dying
141 patients. In fact, medical and nursing schools worldwide have traditionally had a limited emphasis
142 on EoL care [34]. However, PC and EoL issues are not an easy conversation between attending
143 physician and patient or caregivers. Consequently, many of them relate that they have encountered
144 important ethical dilemmas in managing refractory symptoms, discontinuing life-sustaining
145 therapies in dying patients [35], and, especially, considering palliative sedation [36].

146 Evidence from clinical studies suggest that patients with end-stage diseases are often treated
147 during hospitalization with aggressive medical intervention, including prolonged ICU stay, rather
148 than with PC [22,28]. Often, the care that these patients receive during ICU stay is more aimed
149 towards prolongation of their lives, rather than to palliation of symptoms [37]. Similarly, aggressive
150 EoL care in the last weeks of life of advanced cancer patients, such as chemotherapy administration
151 or ICU admission are commonly deemed markers of poor quality care [38].

152 It is of concern that caregivers of patients receiving aggressive care are at higher risk of
153 experiencing a major depressive disorder, and in general a worse QoL, likely because they are
154 unprepared to the death of their relatives [39]. Several studies pointed out that one barrier to
155 providing quality care at the EoL was the lack of communication between the patient/family and the
156 medical team [40]. It has been shown that most of patients would like to have a discussion with
157 their physicians about EoL care, but this often remained an unmet issue [41,42].

158 In order to better manage patients with end-stage disease or advanced cancer in the recent
159 years hospital-based PC programs have been developed [43,44]. Specifically, the aim of these
160 programs is to improve symptom management, help patients and families in better understand
161 prognosis and treatment options, clarify goals of care, and assist in planning of care as the disease
162 progresses.

163 Several studies indicated that hospital-based PC services increased satisfaction of patients and
164 families [45], improved QoL [46], reduced ICU length of stay [47], and decreased costs [48,49]. In
165 a very recent review, the authors have underlined the advantages of a PC-oriented approach in
166 improving patient's outcomes, including symptom burden, QoL, and EoL outcomes, all achieved
167 with lower associated costs [50].

168

169 **5. How do they work inhospital palliative care services?**

170 Within hospitals, the primary model of PC delivery is the multidisciplinary consultation team,
171 which should be composed of physicians, nurses, and psychologists trained in PC, with the support
172 of specialty physicians (geriatrician, internist, physiatrist, neurologist, psychiatrist) and other
173 healthcare professionals (dietician, physical therapist, respiratory therapist) as well as pharmacists,
174 social workers, case managers, spiritual counselors, and volunteers [51]. The PC team must have a
175 tight bidirectional communication with home PC services, hospices, and primary care physicians.

176 Indeed, in the United States a PC team is present in almost 90% of hospitals with 300 beds or
177 more and two thirds of hospitals with 50 beds or more [51]. During the last decade, also in Europe,

178 PC programs in hospitals have significantly increased, although much remains to be done in this
179 area.

180 The PC team provides consultations to inpatients, working with attending healthcare
181 professionals to ensure patient's focused and family's centered care. The most important purpose of
182 the team is to achieve the best possible QoL for both patients and their families/caregivers by
183 assessing and managing refractory symptoms [52]. Also, the team facilitates patient's and family's
184 understanding of the underlying disease process and promotes decision-making based on informed
185 choices. Actually, the team should be involved for those cases where management of symptoms
186 requires more than the basic knowledge or communication becomes difficult due to arising
187 conflicts.

188 Both randomized controlled trials and observational studies compared the outcomes in
189 patients with chronic life-limiting diseases who were referred to hospital-based PC teams with those
190 in patients who received usual care and reported reduced symptom burden, improved QoL, and
191 decreased spiritual distress among the patients referred to PC [53-56].

192 For a few years, a new approach in managing patients with end-stage diseases in the hospital
193 context is represented by the Acute Palliative Care Unit (APCU) [57]. The focus of the APCU is
194 rapid symptom control and intensive psychosocial care, with a shorter length of stay and a lower
195 death rate (20-50%) than those in hospice [58]. Therefore, the APCU differs from hospice which
196 offers more extensive long-term PC or exclusively near-death care.

197 The APCU provides intensive PC for inhospital patients and families, with the aim of
198 enhancing QoL, facilitating transition to EoL care, and assisting with hospital discharge. The
199 discharge from the APCU represents an important and complex process, as it must provide a
200 location (e.g., home, hospice, or long-term care facility) in which the patient finds appropriate care
201 until death, avoiding unplanned hospital admissions for lack of symptom management skills [10].
202 The choice of the discharge location depends on availability of caregivers and, mainly, on patient's

203 preferences, performance status, and life expectancy as well as other logistic and financial factors
204 [59].

205 Briefly, the APCU may be the hospital place where to provide patients with end-stage disease
206 or advanced cancer with a personalized medicine tailored to their individual's needs.

207

208 **6. Which is the impact of inhospital palliative care services on cost savings?**

209 The increasing development of medical technology gives to inhospital physicians the
210 opportunity to easily opt for life-prolonging therapies or devices in patients with end-stage disease
211 or advanced cancer; e.g., new combination of adjuvant chemotherapy with targeted drugs, left
212 ventricular assisted devices, mechanical ventilation, haemodialysis, and artificial nutrition.
213 Consequently, these patients frequently undergo various imaging techniques, interventional
214 procedures, and therapies, even near the end of their lives. Such behavior of physicians does neither
215 translate in a better management of the PC patient nor in a better patient's QoL, while often
216 represents a discomfort for the patient and a source of unnecessary costs for the healthcare system.

217 Several studies suggest that PC consultation is associated with cost saving in hospitalized
218 patients, as it allows to identify those patients who would benefit from a palliative approach rather
219 than an aggressive one. Since 2008, Morrison *et al.* stated that hospital PC team consultations were
220 associated with significant hospital cost savings [60]. Starks *et al.* reported that PC team
221 interventions resulted in cost savings for short and medium length of stay, but not for stays more
222 than 30 days; therefore, the authors concluded that cost savings can be achieved by an earlier
223 involvement of the PC team [61].

224 In a recent review Dalal and Bruera have reported that the magnitude of hospital cost savings
225 with PC involvement ranged from 9 to 32% and these savings were higher when PC team was
226 involved earlier (within two days from patient's admission) [50]. Two recent studies [62,63] have
227 pointed out that cancer patients' care was characterized by high-cost and low-value interventions,
228 high hospital readmission rates, prolonged length of stay, hospital deaths, and frequent use of

229 chemotherapy and other disease-centered interventions near the EoL. These data are indicative of
230 poor care coordination and inadequate EoL planning, and such a management translates into costs
231 escalation, while patients continue to receive nonbeneficial and burdensome health interventions at
232 the EoL. These studies demonstrated that referral to PC team improved various healthcare
233 utilizations and quality measures, including 30-day readmission rates, hospice use, and avoiding of
234 chemotherapy following discharge.

235

236 **7. Conclusions**

237 The attitudes and knowledge of healthcare professionals towards PC may exert influence on
238 their communication with patients and caregivers and, mainly, on patients' quality of care near the
239 EoL. Therefore, the best management of PC for hospitalized patients with end-stage disease or
240 advanced cancer should be based on a well-defined cooperation between PC team and treating
241 physicians. Actually, multidisciplinary PC teams aim to address the full spectrum of patients'
242 health, spiritual, and psychosocial needs, and match treatment choices with patients' values and
243 will.

244 In conclusion, we sincerely believe that to improve the care of these inpatients with relevant
245 symptom burden, particularly after an unplanned hospital admission or when the patient is dying,
246 each hospital should ensure that professionals expert in PC are available to support treating
247 physicians.

248

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250 A. De Luca revised the manuscript critically for important intellectual content. All authors approved
251 the final manuscript.

252

253 **Conflicts of Interest:** The authors declare no conflict of interest.

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255 **References**

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257 1. World Health Organization Definition of Palliative Care. Available online URL:
258 <http://www.who.int/mediacentre/factsheets/fs402/en/> (accessed on 3 October 2017).

259 2. Gómez-Batiste X., Martínez-Munoz M., Blay C., Espinosa J., Contel J.C., Ledesma A.
260 Identifying needs and improving palliative care of chronically ill patients: a community-oriented,
261 population-based, public-health approach. *Curr. Opin. Support. Palliat. Care* **2012**, *6*, 371-378.
262 [DOI: 10.1097/SPC.0b013e328356aaed]

263 3. Higginson I.J., Addington-Hall J.M. Palliative care needs to be provided on basis of needs
264 rather than diagnosis. *B.M.J.* **1999**, *318*, 123. [PMID: 9880293]

265 4. Global atlas of palliative care at the end of life. Connor, S.R., Sepulveda Bermedo, M.C.,
266 Eds.; World Health Organization, **2014**, pp 1-111. ISBN: 978-0-9928277-0-0. Available online
267 URL: http://www.who.int/nmh/Global_Atlas_of_Palliative_Care-pdf (accessed on 3 October 2017).

268 5. Solano J.P., Gomes B., Higginson I.J. A comparison of symptom prevalence in far advanced
269 cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. *J. Pain*
270 *Symptom. Manage.* **2006**; *31*, 58-69. [DOI: 10.1016/j.jpainsymman.2005.06.007]

271 6. Barbera L., Taylor C., Dudgeon D. Why patients with cancer visit the emergency
272 department near the end of life? *C.M.A.I.* **2010**, *182*, 563-568. [DOI: 10.1503/cmaj.091187]

273 7. Smith A.K., Fisher J., Schonberg M.A., Pallin D.J., Block S.D., Forrow L., Phillips R.S.,
274 McCarthy E.P. Am I doing the right thing? Provider perspectives on improving palliative care in the
275 emergency department. *Ann. Emerg. Med.* **2008**, *54*, 86-93. [DOI:
276 10.1016/j.annemergmed.2008.08.022]

277 8. Siegel M., Biegelow S. Palliative care symptom management in the emergency department:
278 the ABC's of symptom management for the emergency physician. *J. Emerg. Med.* **2017**, pii: S0736-
279 4679(17)30705-9. [DOI: 10.1016/j.jemermed.2017.08.004]

- 280 9. Van Mechelen W., Aertgeerts B., De Ceulaer K., Thoonsen B., Vermandere M.,
281 Warmenhoven F., Van Rijswijk E., De Lepeleire J. Defining the palliative care patient: A
282 systematic review. *Palliat. Med.* **2013**, *27*, 197-208. [DOI: 10.1177/0269216311435268]
- 283 10. Gardiner C., Ingleton C., Gott M., Ryan T. Exploring the transition from curative care to
284 palliative care: a systematic review of the literature. *B.M.J. Support. Palliat. Care* **2011**, *1*, 56-63.
285 [DOI: 10.1136/bmjspcare-2010-000001]
- 286 11. Gott M., Ingleton C., Bennett M.I., Gardiner C. Transitions to palliative care in acute
287 hospitals in England: qualitative study. *B.M.J.* **2011**, *342*, d1773. [DOI: 10.1136/bmjspcare-2010-
288 000001]
- 289 12. Bruera E. Emergency department point of palliative care access for patients with advanced
290 cancer. *J.A.M.A. Oncol.* **2016**, *2*, 577-578. [DOI: 10.1001/jamaoncol.2015.5321]
- 291 13. George N.R., Kryworuchko J., Hunold K.M., Ouchi K., Berman A., Wright R., Grudzen
292 C.R., Kovalerchik O., LeFebvre E.M., Lindor R.A., Quest T.E., Schmidt T.A., Sussman T.,
293 Vandenbroucke A., Volandes A.E., Platts-Mills T.F. Shared decision making to support the
294 provision of palliative and end-of-life care in the emergency department: A consensus statement
295 and research agenda. *Acad. Emerg. Med.* **2016**, *23*, 1394-1402. [DOI: 10.1111/acem.13083]
- 296 14. Cotogni P., De Luca A., Evangelista A., Filippini C., Gili R., Scarmozzino A., Ciccone G.,
297 Brazzi L. A simplified screening tool to identify seriously ill patients in the Emergency Department
298 for referral to a palliative care team. *Minerva Anesthesiol.* **2017**, *83*, 474-484. [DOI:
299 10.23736/S0375-9393.16.11703-1]
- 300 15. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Palliative Care.
301 Version 2. 2017. Available online URL:
302 https://www.nccn.org/professionals/physician_gls/pdf/palliative.pdf (accessed on 3 October 2017).
- 303 16. SIAARTI - Italian Society of Anaesthesia Analgesia Resuscitation and Intensive Care.
304 Grandi insufficienze d'organo "end stage": cure intensive o cure palliative? "Documento
305 Condiviso" per una pianificazione delle scelte di cura. **2013**; pp 1-60. Available online URL:

- 306 <http://www.siaarti.it/News/grandi-insufficienze-organo-end-stage-cure-intensive-o-cure->
307 [palliative.aspx](http://www.siaarti.it/News/grandi-insufficienze-organo-end-stage-cure-intensive-o-cure-palliative.aspx) (accessed on 3 October 2017).
- 308 17. Wu F.M., Newman J.M., Lasher A., Brody A.A. Effects of initiating palliative care
309 consultations in the emergency department on inpatient length of stay. *J. Palliat. Med.* **2013**, *16*,
310 1362–1367. [DOI: 10.1089/jpm.2012.0352]
- 311 18. Grudzen C.R., Richardson L.D., Johnson P.N., Hu M., Wang B., Ortiz J.M., Kistler E.A.,
312 Chen A., Morrison R.S. Emergency department-initiated palliative care in advanced cancer: A
313 randomized clinical trial. *J.A.M.A. Oncol.* **2016**, *2*, 591-598. [DOI: 10.1001/jamaoncol.2015.5252]
- 314 19. Cotogni P., De Luca A., Saini A., Brazzi L. Unplanned hospital admissions of palliative care
315 patients: a great challenge for internal and emergency medicine physicians. *Intern. Emerg. Med.*
316 **2017**, *12*, 569-571. [DOI: 10.1007/s11739-017-1671-3]
- 317 20. Cohen J., Bilsen J., Addington-Hall J., Lofmark R., Miccinesi G., Kaasa S., Deliens L.
318 Population-based study of dying in hospital in six European countries. *Palliat. Med.* **2008**, *22*, 702-
319 710. [DOI: 10.1177/0269216308092285]
- 320 21. [No authors listed]. A controlled trial to improve care for seriously ill hospitalized patients.
321 The study to understand prognoses and preferences for outcomes and risks of treatments
322 (SUPPORT). The SUPPORT Principal Investigators. *J.A.M.A.* **1995**, *274*, 1591-1598. [PMID:
323 7474243]
- 324 22. Ahronheim J.C., Morrison R.S., Baskin S.A., Morris J., Meier D.E.: Treatment of the dying
325 in the acute care hospital. Advanced dementia and metastatic cancer. *Arch. Intern. Med.* **1996**, *156*,
326 2094-2100. [PMID: 8862102]
- 327 23. Baker R., Wu A.W., Teno J., Kreling B., Damiano A.M., Rubin H.R., Roach M.J., Wenger
328 N.S., Phillips R.S., Desbiens N.A., Connors A.F. Jr, Knaus W., Lynn J. Family satisfaction with
329 end-of-life care in seriously ill hospitalized adults. *J. Am. Geriatr. Soc.* **2000**, *48*, S5, S61–S69.
330 [PMID: 10809458]

- 331 24. Mularski R.A., Heine C.E., Osborne M.L., Ganzini L., Curtis J.R. Quality of dying in the
332 ICU: Ratings by family members. *Chest* **2005**, *128*, 280-287. [PMID: 16002947]
- 333 25. Teno J.M., Clarridge B.R., Casey V., Welch L.C., Wetle T., Shield R., Mor V. Family
334 perspectives on end-of-life care at the last place of care. *J.A.M.A.* **2004**, *291*, 88-93. [PMID:
335 14709580]
- 336 26. Claessens M.T., Lynn J., Zhenshao Z., Desbiens N.A., Phillips R.S., Wu A.W., Harrell F.E.
337 Jr, Connors A.F. Jr. Dying with lung cancer or chronic obstructive pulmonary disease. Insights from
338 SUPPORT. *J. Am. Geriatr. Soc.* **2000**, *48*, S146-S153. [PMID: 10809468]
- 339 27. Lynn J., Teno J.M., Phillips R.S., Wu A.W., Desbiens N., Harrold J., Claessens M.T.,
340 Wenger N., Kreling B., Connors A.F. Jr. Perceptions by family members of the dying experience of
341 older and seriously ill patients. SUPPORT Investigators. Study to Understand Prognoses and
342 Preferences for Outcomes and Risks of Treatments. *Ann. Intern. Med.* **1997**, *126*, 97-106. [PMID:
343 9005760]
- 344 28. Teno J.M., Fisher E., Hamel M.B., Wu A.W., Murphy D.J., Wenger N.S., Lynn J., Harrell
345 F.E. Jr. Decision making and outcomes of prolonged ICU stay in seriously ill patients. *J. Am.*
346 *Geriatr. Soc.* **2000**, *48*, S70-74. [PMID: 10809459]
- 347 29. Weiner J.S., Cole S.A. Three principles to improve clinician communication for advance
348 care planning: overcoming emotional, cognitive, and skill barriers. *J. Palliat. Med.* **2004**, *7*, 817-
349 829. [DOI: 10.1089/jpm.2004.7.817]
- 350 30. Tulsky J.A. Beyond advance directives: Importance of communication skills at the end of
351 life. *J.A.M.A.* **2005**, *294*, 359-365. [DOI:]
- 352 31. Miller S.C., Kinzbrunner B., Pettit P., Williams J.R. How does the timing of hospice referral
353 influence hospice care in the last days of life? *J. Am. Geriatr. Soc.* **2003**, *5*, 798-806. [DOI:]
- 354 32. Shocklett E.R., Teno J.M., Miller S.C., Stuart B. Late referral to hospice and bereaved
355 family member perception of quality of end-of-life care. *J. Pain. Symptom. Manage.* **2005**, *3*, 400-
356 407. [DOI: 10.1001/jama.294.3.359]

- 357 33. Muir J.C., Arnold R.M. Palliative care and the hospitalist: an opportunity for cross-
358 fertilization. *Am. J. Med.* **2001**, *111*, 10S-14S. [PMID: 11790362]
- 359 34. Block S.D. Medical education in end-of-life care: the status of reform. *J. Palliat. Med.* **2002**,
360 *5*, 243-248. [PMID: 12006224]
- 361 35. Kinzbrunner B.M. Ethical dilemmas in hospice and palliative care. *Support. Care Cancer*
362 **1995**, *3*, 28–36. [PMID: 7535167]
- 363 36. Cotogni P., Brazzi L. Palliative sedation: a feasible option to improve end-of-life care in
364 seriously ill dying patients. *Minerva Anesthesiol.* **2017**, *83*, 446-448. [DOI: 10.23736/S0375-
365 9393.17.11906-1]
- 366 37. Au D.H., Udris E.M., Fihn S.D., McDonnell M.B., Curtis J.R. Differences in health care
367 utilization at the end of life among patients with chronic obstructive pulmonary disease and patients
368 with lung cancer. *Arch. Intern. Med.* **2006**, *166*, 326-331. [DOI: 10.1001/archinte.166.3.326]
- 369 38. Rocque G.B., Barnett A.E., Illig L., Eickhoff J.C., Bailey H.H., Vampbell T.C., Stewart
370 J.A., Cleary J.F. Inpatient hospitalization of oncology patients: are we missing an opportunity for
371 end-of-life care? *J. Oncol. Pract.* **2013**, *9*, 51–54. [DOI: 10.1200/JOP.2012.000698]
- 372 39. Wright, A. A. Zhang B., Ray A., Mack J.W., Trice E., Balboni T., Mitchell S.L., Jackson
373 V.A., Block S.D., Maciejewski P.K., Prigerson H.G. Associations between end-of-life discussions,
374 patient mental health, medical care near death, and caregiver bereavement adjustment. *J.A.M.A.*
375 **2008**, *300*, 1665–1673. [DOI: 10.1001/jama.300.14.1665]
- 376 40. Mack, J. W., Smith, T. J. Reasons why physicians do not have discussions about poor
377 prognosis, why it matters, and what can be improved. *J. Clin. Oncol.* **2012**, *30*, 2715–2717. [DOI:
378 10.1200/JCO.2012.42.4564]
- 379 41. Hagerty R.G., Butow P.N., Ellis P.M., Lobb E.A., Pendlebury S.C., Leigh N., MacLeod C.,
380 Tattersall M.H. Communicating with realism and hope: incurable cancer patients' views on the
381 disclosure of prognosis. *J. Clin. Oncol.* **2005**, *23*, 1278–1288. [DOI: 10.1200/JCO.2005.11.138]

- 382 42. Steinhauser K.E., Christakis N.A., Clipp E.C., McNeilly M., Grambow S., Parker J., Tulsky
383 J.A. Preparing for the end of life: preferences of patients, families, physicians, and other care
384 providers. *J. Pain. Symptom. Manage.* **2001**, *22*, 727–737. [PMID: 11532586]
- 385 43. Manfredi P.L., Morrison R.S., Morris J., Goldhirsch S.L., Carter J.M., Meier D.E. Palliative
386 care consultations: how do they impact the care of hospitalized patients? *J. Pain. Symptom.*
387 *Manage.* **2000**, *20*, 166-173. [PMID: 11018334]
- 388 44. Pan C.X., Morrison R.S., Meier D.E., Natale D.K., Goldhirsch S.L., Kralovec P., Cassel
389 C.K. How prevalent are hospital-based palliative care programs? Status report and future directions.
390 *J. Palliat. Med.* **2001**, *4*, 315-324. [DOI: 10.1089/109662101753123922]
- 391 45. Dy S.M., Shugarman L.R., Lorenz K.A., Mularski R.A., Lynn J. RAND-Southern California
392 Evidence-Based Practice Center. A systematic review of satisfaction with care at the end of life. *J.*
393 *Am. Geriatr. Soc.* **2008**, *56*, 124-129. [DOI: 10.1111/j.1532-5415.2007.01507.x]
- 394 46. Morrison R.S. Health care system factors affecting end-of-life care. *J. Palliat. Med.* **2005**, *8*,
395 S79-S87. [DOI: 10.1089/jpm.2005.8.s-79]
- 396 47. Back A.L., Li Y.F., Sales A.E. Impact of palliative care case management on resource use
397 by patients dying of cancer at a Veterans Affairs medical center. *J. Palliat. Med.* **2005**, *8*, 26-35.
398 [DOI: 10.1089/jpm.2005.8.26]
- 399 48. Brumley R., Enguidanos S., Jamison P., Seitz R., Morgenstern N., Saito S., McIlwane J.,
400 Hillary K., Gonzalez J. Increased satisfaction with care and lower costs: results of a randomized
401 trial of in-home palliative care. *J. Am. Geriatr. Soc.* **2007**; *55*, 993-1000. [DOI: 10.1111/j.1532-
402 5415.2007.01234.x]
- 403 49. Gade G., Venohr I., Conner D., McGrady K., Beane J., Richardson R.H., Williams M.P.,
404 Liberson M., Blum M., Della Penna R. Impact of an inpatient palliative care team: a randomized
405 control trial. *J. Palliat. Med.* **2008**; *11*, 180-190. [DOI: 10.1089/jpm.2007.0055]
- 406 50. Dalal S., Bruera E. End-of-life care matters: palliative cancer care results in better care and
407 lower costs. *Oncologist*, **2017**; *22*, 361-368. [DOI: 10.1634/theoncologist.2016-0277]

- 408 51. Kelly A.S., Morrison R.S. Palliative care for the seriously ill. *N. Engl. J. Med.* **2015**, *373*,
409 747-755. [DOI: 10.1056/NEJMra1404684]
- 410 52. Wilkinson E.K., Salisbury C., Bosanquet N., Franks P.J., Kite S., Lorentzon M., Naysmith
411 A. Patient and carer preference for, and satisfaction with, specialist models of palliative care: a
412 systematic literature review. *Palliat. Med.* **1999**, *13*, 197-216. [DOI:
413 10.1191/026921699673563105]
- 414 53. Higginson I.J., Finlay I., Goodwin D.M., Cook A.M., Hood K., Edwards A.G., Douglas
415 H.R., Norman C.E. Do hospital-based palliative teams improve care for patients or families at the
416 end of life? *J. Pain. Symptom. Manage.* **2002**, *23*, 96-106. [PMID: 11844629]
- 417 54. Bakitas M., Lyons K.D., Hegel M.T., Balan S., Brokaw F.C., Seville J., Hull J.G, Li Z.,
418 Tosteson T.D., Byock I.R., Ahles T.A. Effects of a palliative care intervention on clinical outcomes
419 in patients with advanced cancer: the Project ENABLE II randomized controlled trial. *J.A.M.A.*
420 **2009**, *302*, 741-749. [DOI: 10.1001/jama.2009.1198.]
- 421 55. Temel J.S., Greer J.A., Muzikansky A., Gallagher E.R., Admane S., Jackson V.A., Dahlin
422 C.M., Blinderman C.D., Jacobsen J., Pirl W.F., Billings J.A., Lynch T.J. Early palliative care for
423 patients with metastatic non-small-cell lung cancer. *N. Engl. J. Med.* **2010**, *363*, 733-42. [DOI:
424 10.1056/NEJMoa1000678.]
- 425 56. Balboni T.A., Vanderwerker L.C., Block S.D., Paulk M.E., Lathan C.S., Peteet J.R.,
426 Prigerson H.G. Religiousness and spiritual support among advanced cancer patients and
427 associations with end-of-life treatment preferences and quality of life. *J. Clin. Oncol.* **2007**, *25*, 555-
428 560. [DOI: 10.1200/JCO.2006.07.9046]
- 429 57. Eti S., O'Mahony S., McHugh M., Guilbe R., Blank A., Selwyn P. Outcomes of the acute
430 palliative care unit in an academic medical centre. *Am. J. Hosp. Palliat. Med.* **2014**, *31*, 380-384.
431 [DOI: 10.1177/1049909113489164]
- 432 58. Shin S.H., Hui D., Chisholm G.B., Kwon J.H., San Miguel M.T., Allo J.A. Yennurajalingam
433 S., Frisbee-Hume S.E., Bruera E. Characteristics and outcomes of patients admitted to an acute

- 434 palliative care unit from the emergency centre. *J. Pain. Symptom. Manage.* **2014**, *47*, 1028-1034.
435 [DOI: 10.1016/j.jpainsymman.2013.07.015]
- 436 59. Hui D., Elsayem A., Palla S., De La Cruz M., Li Z., Yennurajalingam S., Bruera E.
437 Discharge outcomes and survival of patients with advanced cancer admitted to an acute palliative
438 care unit at a comprehensive cancer centre. *J. Palliat. Med.* **2010**, *13*, 49-57. [DOI:
439 10.1089/jpm.2009.0166]
- 440 60. Morrison R.S., Penrod J.D., Cassel J.B., Caust-Ellenbogen M., Litke A., Spragens L., Meier
441 D.E. Palliative Care Leadership Centers' Outcomes Group. Cost savings associated with US
442 hospital palliative care consultation programs. *Arch. Intern. Med.* **2008**, *168*, 1783-1790. [DOI:
443 10.1001/archinte.168.16.1783]
- 444 61. Starks H., Wang S., Farber S., Owens D.A., Curtis J.R. Cost savings vary by length of stay
445 for inpatients receiving palliative care consultation services. *J. Palliat. Med.* **2013**, *16*, 1215-1220.
446 [DOI: 10.1089/jpm.2013.0163]
- 447 62. Adelson K., Paris J., Horton J.R., Hernandez-Tellez L., Ricks D., Morrison R.S., Smith C.B.
448 Standardized criteria for palliative care consultation on a solid tumor oncology service reduces
449 downstream health care use. *J. Oncol. Pract.* **2017**, *13*, e431-e440. [DOI:
450 10.1200/JOP.2016.016808]
- 451 63. Triplett D.P., LeBrett W.G., Bryant A.K., Bruggeman A.R., Matsuno R.K., Hwang L.,
452 Boero I.J., Roeland E.J., Yeung H.N., Murphy J.D. Effect of palliative care on aggressiveness of
453 end-of-life care among patients with advanced cancer. *J. Oncol. Pract.* **2017**, *13*, e760-e769. [DOI:
454 10.1200/JOP.2017.020883]