Efficacy of Advance Directive Education on the Completion of Living Will in Chronically ILL Patients: An Evidence-Based Care Report

Jessica¹, Edward Faisal²

¹Faculty of Medicine, Universitas Indonesia;

²Psychosomatic and Palliative Division, Internal Medicine Department, Cipto Mangunkusumo Hospital, Faculty of Medicine,

Universitas Indonesia.

Corespondency: Edward Faisal. Psychosomatic and Palliative Division, Departement of Internal Medicine, Faculty of Medicine, Universitas Indonesia/Cipto Mangunkusumo Hospital. Jl. Diponegoro No. 71, Jakarta, Indonesia.

Abstract:-

Background: Advance directive (AD) is an important part in palliative care because it can increase patient's quality of life and helps with a dignified death but currently it is still not well-known or widespread within the general population.

Objective: To find if education about AD increases the completion of living will in chronically ill patients.

Methods: A literature search was performed on 13 August 2021 with 263 articles found. After manual title screening and duplicate removal, 5 articles were selected and critically appraised with 2010 CEBM Oxford criteria.

Result: In Chung et al, education about AD increases the completion of living will from 10.26% to 35.94%. In Courtright et al 70-80% patients were interested in making AD after education about AD with completion rates of 13.1% and 12.2% for each group. In Halpern et al completion rates were 50.66%, 55.15%, and 55.35% for each group; and meta-analysis in Houben et al results in a favorable odds ratio (OR= 3,26; 95% CI= 2,00-5,32; P < 0,00001).

Conclusion: Education about AD increases patient's willingness to create and eventually complete AD/living will and the concordance of written AD with medical procedures that the patient receives.

Keywords:- Advance Directive, Education, Living Will Completion.

I. INTRODUCTION

Case Illustration:

A 42-year-old male was diagnosed with anaplastic thyroid carcinoma 2 months ago. Patient underwent thyroidectomy and supportive therapy, but recent PET-CT result showed distant metastases in the bones and lungs. Patient is a single father with 3 children and all of his children are below 10 years of age. Patient is the third child of five siblings, however both of patient's parents have passed away and all of his siblings live abroad. Patient is still in a relatively good condition but is concerned about his worsening illness making him unable to make decisions by himself in the future.

Background:

Palliative care is an approach to increase the quality of life and help with a dignified death in patients with cancer, chronic illness, or other terminal condition that starts when a patient is diagnosed, continues during treatment until the patient dies and when the patient's family is grieving.[1,2] Palliative care is done comprehensively and involves not only healthcare workers, but also other non-medical parties such as the patient himself/herself, therapist, social worker and even religious support.[1]

One important aspect in palliative care is Advance Directive (AD). Advance directive is a written document with clear direction of which medical assistance a person wishes to get or refuse when that person becomes unable to make a decision for himself/herself.[1,3] Advance Directive was first developed after some civil cases involving life support discontinuation such as the cases of Karen Ann Quinlan and Nancy Cruzan[4,5] which sparked the importance of living will to prevent cases like those where a person is unable to make a decision by himself/herself.[4]

Advance Directive is done based mostly on the autonomy principle but also considering other principles of medical ethics such as beneficence, justice, and non-maleficence.[6,7] The development of medical technology creates the potential of unnecessary treatments that can prolong the suffering of a patient, thus not fulfilling the principles of palliative care.[6] Patients with a completed AD can avoid this by clearly stating which medical assistance he/she wishes to get or refuse to achieve a dignified death without prolonging suffering.[5,6]

Even though AD is an important part in palliative care, in practice the completion rate of AD remains low even in palliative population, where the completion rates are barely higher compared to healthy population.[3,5,8] Many factors can hinder the completion of AD, such as the lack of knowledge about AD, patient's procrastination in making AD, patient's difficulty in discussing negative topics or death, uncertainty whether AD will actually make a difference in end of life care, waiting for medical professional to initiate AD discussion, and patient's preference for other parties such as

ISSN No:-2456-2165

family or physician to make decisions for him/her, with the last factor happening in both eastern and western countries.[5] Some of those factors are related to AD education, hence the education of AD is expected to increase the completion rates of AD.

II. METHODS

Clinical Question:

Does Advance Directive education increase the completion rates of living will in patients with chronic diseases?

P: Patients with chronic illness

I: Advance directive education

C: No education

O: Living will completion

Type of clinical question: Intervention

Study design: Retrospective Cohort, Randomized Clinical Trial (RCT)

Search Method and Databases

A literature search was performed on 13 August 2021 on the MEDLINE, PubMed, Cochrane, and ProQuest databases. The following keywords were used: advance directive; chronic illness; will completion; attitude; survivor; qualitative. The keywords were combined with the word AND or NOT. (Figure 1)

Article Selection

Articles had to meet the following criteria to be included in the critical appraisal: (1) published within 10 years of the search date; (2) has cancer patients as research subject; (3) has other severe chronic illness as research subject. Articles containing research protocols or qualitative studies were excluded from the critical appraisal. In total, 94 articles were found in PubMed, 78 in Medline, 91 in ProQuest, but no articles were found in Cochrane. After a manual title and abstract screening and duplicates removal, 4 articles selected. A manual search on Google Scholar was then done to find meta-analysis articles with 1 article as a result. In total, 5 articles were included in the critical appraisal, with 1 cohort article, 2 randomized control trial articles, and 2 systematic review articles. Articles were then appraised with 2010 Centre for Evidence-Based Medicine (CEBM) University of Oxford criteria.

III. RESULTS

Validity

The validity of each study can be seen on table 1, 2, and 3.

Importance

In Chung et al[9] 20 out of 195 (10.26%) patients had an AD before being admitted to the emergency room before the bill was passed and 78 out of 217 (35.94%) after the bill was passed. Statistical analysis shows a significant difference in the length of stay in ER (p=0.042), referral from ER (p=0.020), and survival after discharge from ER (p=0.001). (Figure 2)

In Courtright et al[10] 115 from 160 (71.9%) patients in standard choice group and 133 from 156 (85.3%) in expanded

choice group were interested in making AD. After follow-up was done, 21 patients (13.1% of total, 18.3% of those interested) in standard choice group and 19 patients (12.2% of total, 14.3% of those interested) in expanded choice group. Combined, 40 out of 316 (12.7% from total, 31.25% from those interested. There is no significant difference in the AD completion rate between the two groups (P= 0.40; 95% CI: 8.8-21.4%). (Figure 3)

In Halpern et al[11] 85 out of 168 (50.06%) patients in comfort AD group, 91 out of 165 (55.15%) in standard AD group, and 88 out of 159 (55.35%) in life-extending AD group completed an AD. Patients in each group tend to choose the same type of AD as the randomization group (P=0.001). (Figure 4) In the modified intention-to-treat (mITT) analysis there is no significant difference between medical outcome between standard AD and comfort AD (RR= 1.05; 95% CI, 0.90–1.23; P < .001) and also no significant difference between standard AD and life-extending AD (1.03; 95% CI, 0.88–1.20; P < .001), evaluated by the amount of hospital free days.(Figure 5)

In Mackenzie et al[12] there is evidence that AD education with the Respecting Choices protocol increases AD completion and consistency perception between patient and patient's surrogate but no clear evidence for quality of life improvement and concordance between AD and the actual medical assistance a patient receives. There is no meta-analysis done in this study.

In Houben et al[13] 3 outcomes were evaluated with significant results: AD completion from 9 RCTs (OR= 3.26; 95% CI= 2.00-5.32; P < 0.00001); (Figure 6) number of discussion about end-of-life preferences from 11 RCTs (OR= 2.82; 95% CI= 2.09-3.79; P < 0.00001); and the concordance between patient's AD and the actual medical assistance a patient receives (OR= 4.66; 95% CI= 1.20-18.08; P= 0.03). (Figure 7) However, 55.4% of studies analyzed were classified as low-quality RCTs due to the lack of blinding in both patients and researchers or due to the low number of samples.

Applicability

All studies appraised showed that AD education increases the completion rates of AD.

IV. DISCUSSION

The patient described has anaplastic thyroid carcinoma and is worried that his condition will make him unable to make a decision by his own in the future. According to the available data, anaplastic thyroid carcinoma has a 1-year survival rate of 25% and 2-year survival rate of 6.3% in cases with distant metastases and overall 5-year survival rate of 4.7%.[14]

The prevalence of AD in adult population varies between countries, with 14% in Australia[15], 0.5% in Hong Kong[16], 1.8% in Belgium[15], 19.3% in Canada[17], 16.4% in nursing home population in Taiwan[18], 10% in Chinese-American population in the United States[19], and

36.7% in the general American population[8]. These data show that social environment affects the perception and prevalence of AD where the prevalence of AD is higher in the western world compared to the east and Chinese-American who have been living for more than 20 years in the United States have more knowledge of AD compared to those who has been living shorter due to the acculturation process with the western culture where AD is more widely known and made.[19]

Research about AD in Asia is still very limited with a low number of both qualitative and quantitative studies, and existing research are still limited to developed countries such as Japan and South Korea, and almost non-existent in poorer regions of Asia. A systematic review by Martina et al showed that the knowledge of AD among healthcare workers in Asia is still low and healthcare workers are still reluctant to start a discussion about AD due to fear of consequence from patient's family and fear of legal consequences.[20] Martina et al also showed that the initiation of AD in Asia is still relatively late due to the majority of AD being made when the patient is in critical condition even though the ideal time for AD to be made is when a patient is first diagnosed.[20] In Southeast Asia research about AD remains very limited with most of research done in Singapore where healthcare workers get training about AD and widespread awareness about AD exists in the general population.[20-22] However, in other Southeast Asian countries AD is still highly debated and research is still limited to research about perception especially in countries with highly religious population such as Malaysia and The Philippines. [23,24] We cannot find articles about AD from other Southeast Asian countries and for Indonesia we can only find a literature review article.[3] We hope that AD awareness will increase in the future, not only within healthcare workers but also in the general population and if possible made into a law in more countries.

The low prevalence of AD in the general population can be attributed to the lack of knowledge about AD and its benefits, where the majority of respondents either did not know about AD or have never heard about AD[16], or have heard a little about AD but have misconceptions about AD[19,25]. Conversely, in respondents who have heard or have a good knowledge of AD, 70-80% of them have a positive opinion about AD and have expressed eagerness to create an AD in the future[16,25]. Similar thing was observed in the studies appraised in this article, where the majority of patients who got education about AD wanted to make an AD[10,11,13].

Even though the knowledge about AD increases the number of individuals interested in making an AD, it is just one of the things that can hinder the completion of AD.[5,14] Other factors that can hinder the includes culture, education level, certain beliefs, lack of interest to create AD, and misconceptions about AD both in the general population and healthcare workers[21,26–28], difference of opinion between patient and patient's surrogate, availability of palliative care, and even lack of documentation of AD[5,29]. Many of factors are related to the socioeconomic circumstances of a patient, and the effect is greater in minority population[30] which is

disproportionately poorer[31] and tends to have beliefs that conflicts with the principle of AD[29,32–34]. In research by Shen et al about AD which compares the completion of AD between Latino and non-Latino population, education about AD decreases the disparity between the two groups.[32] In the articles appraised in this EBCR, there are statistical analysis with adjustment for minority populations[10,11] and in MacKenzie at al includes articles that focus on minority populations[12]. However AD completion is still a challenge even without those factors with the amount of patients not completing AD even after multiple follow-up attempts both by direct face-to-face contact and via phone call by the research staff.[10]

Even after an AD is made there are still challenges in the implementation of the completed AD, which is the last obstacle that needs to overcome for a patient to achieve a dignified death.[29] Some factors which can hinder the implementation of a completed AD are the lack of palliative care in the residence or healthcare facility where the patient is, legal status of AD if patient's surrogate does not agree with the AD, and even miscommunication between healthcare facilities or healthcare workers especially in patients who need multidiscipline care. [30,35] In the systematic review by Houben et al[13] there are evidence from 3 studies that the making and completion of AD increases the concordance between the written AD and the actual medical assistance a patient gets but in MacKenzie et al the evidence is heterogenous[12]. Other factors which can affect the concordance of AD includes the changing attitude of a patient during the course of therapy of the disease which can make the already written AD not match with patient's current or future wishes [36,37] and this poses as an important thing for medical workers to always keep communicating with the patient in every encounter and to think of AD as a dynamic thing.[13] This is important because one of the misconceptions about AD is that AD cannot be change after it is made.[38,39]

V. CONCLUSIONS

The articles appraised showed that the education about AD increases the likelihood of a patient to start creating and completing AD and also increases the concordance between the completed AD and the medical assistance a patient receives.

REFRENCES

- [1]. Kementerian Kesehatan Republik Indonesia. Modul TOT Paliatif Kanker Bagi Tenaga Kesehatan. 2016;
- [2]. World Health Organization, editor. National cancer control programmes: policies and managerial guidelines. 2nd ed. Geneva: World Health Organization; 2002.
- [3]. Shatri H, Faisal E, Putranto R, Sampurna B. Advanced Directives pada Perawatan Paliatif. Jurnal Penyakit Dalam Indonesia 2020;7:125–32.
- [4]. Agarwal R, Epstein AS. Advance Care Planning and End-of-Life Decision Making for Patients with Cancer. Seminars in Oncology Nursing 2018;34:316–26.

- [5]. McDonald JC, du Manoir JM, Kevork N, Le LW, Zimmermann C. Advance directives in patients with advanced cancer receiving active treatment: attitudes, prevalence, and barriers. Support Care Cancer 2017;25:523–31.
- [6]. Pérez M del V, Macchi MJ, Agranatti AF. Advance directives in the context of end-of-life palliative care. Current Opinion in Supportive & Palliative Care 2013;7:406–10.
- [7]. Akdeniz M, Yardımcı B, Kavukcu E. Ethical considerations at the end-of-life care. SAGE Open Medicine 2021;9:205031212110009.
- [8]. Yadav KN, Gabler NB, Cooney E, Kent S, Kim J, Herbst N, et al. Approximately One In Three US Adults Completes Any Type Of Advance Directive For End-Of-Life Care. Health Affairs 2017;36:1244–51.
- [9]. Chung YJ, Park I, Cho J, Beom JH, Lee JE. Consent for withholding life-sustaining treatment in cancer patients: a retrospective comparative analysis before and after the enforcement of the Life Extension Medical Decision law. BMC Med Ethics 2021;22:72.
- [10]. Courtright KR, Madden V, Gabler NB, Cooney E, Kim J, Herbst N, et al. A Randomized Trial of Expanding Choice Sets to Motivate Advance Directive Completion. Med Decis Making 2017;37:544–54.
- [11]. Halpern SD, Small DS, Troxel AB, Cooney E, Bayes B, Chowdhury M, et al. Effect of Default Options in Advance Directives on Hospital-Free Days and Care Choices Among Seriously III Patients: A Randomized Clinical Trial. JAMA Netw Open 2020;3:e201742.
- [12]. MacKenzie MA, Smith-Howell E, Bomba PA, Meghani SH. Respecting Choices and Related Models of Advance Care Planning: A Systematic Review of Published Evidence. Am J Hosp Palliat Care 2018;35:897–907.
- [13]. Houben CHM, Spruit MA, Groenen MTJ, Wouters EFM, Janssen DJA. Efficacy of Advance Care Planning: A Systematic Review and Meta-Analysis. Journal of the American Medical Directors Association 2014;15:477–89.
- [14]. Liu T-R, Xiao Z-W, Xu H-N, Long Z, Wei F-Q, Zhuang S-M, et al. Treatment and Prognosis of Anaplastic Thyroid Carcinoma: A Clinical Study of 50 Cases. PLoS ONE 2016;11:e0164840.
- [15]. White B, Tilse C, Wilson J, Rosenman L, Strub T, Feeney R, et al. Prevalence and predictors of advance directives in Australia: Advance directives in Australia. Intern Med J 2014;44:975–80.
- [16]. Chan CWH, Wong MMH, Choi KC, Chan HYL, Chow AYM, Lo RSK, et al. Prevalence, Perception, and Predictors of Advance Directives among Hong Kong Chinese: A Population-based Survey. IJERPH 2019;16:365.
- [17]. Gill GGK, Fukushima E, Abu-Laban RB, Sweet DD. Prevalence of advance directives among elderly patients attending an urban Canadian emergency department. CJEM 2012;14:90–6.
- [18]. Lo Y-T, Wang J-J, Liu L-F, Wang C-N. Prevalence and Related Factors of Do-Not-Resuscitate Directives Among Nursing Home Residents in Taiwan. Journal of

the American Medical Directors Association 2010;11:436–42.

- [19]. Gao X, Sun F, Ko E, Kwak J, Shen H-W. Knowledge of advance directive and perceptions of end-of-life care in Chinese-American elders: The role of acculturation. Pall Supp Care 2015;13:1677–84.
- [20]. Martina D, Lin C-P, Kristanti MS, Bramer WM, Mori M, Korfage IJ, et al. Advance Care Planning in Asia: A Systematic Narrative Review of Healthcare Professionals' Knowledge, Attitude, and Experience. Journal of the American Medical Directors Association 2021;22:349.e1-349.e28.
- [21]. Tee KH, Seet LT, Tan WC, Choo HW. Advance directive: a study on the knowledge and attitudes among general practitioners in Singapore. Singapore Med J 1997;38:145–8.
- [22]. Tay M, Chia SE, Sng J. Knowledge, attitudes and practices of the Advance Medical Directive in a residential estate in Singapore. Ann Acad Med Singap 2010;39:424–8.
- [23]. Malek MM, Saifuddeen SM, Abdul Rahman NN, Mohd Yusof AN, Abdul Majid WR. Honouring Wishes of Patients: An Islamic View on the Implementation of the Advance Medical Directive in Malaysia. MJMS 2021;28:28–38.
- [24]. Martinez RCKP, Rogado MIC, Serondo DJF, Soriano GP, Ilano KCS. Critical Care Nursing in the Philippines. Critical Care Nursing Clinics of North America 2021;33:75–87.
- [25]. De Panfilis L, Rossi PG, Mazzini E, Pistolesi L, Ghirotto L, Noto A, et al. Knowledge, Opinion, and Attitude About the Italian Law on Advance Directives: A Population-Based Survey. Journal of Pain and Symptom Management 2020;60:906-914.e4.
- [26]. Minooka M. [The importance of the advance directive and the difficulties of its prevalence]. Gan To Kagaku Ryoho 2008;35 Suppl 1:41–2.
- [27]. Lipson AR, Hausman AJ, Higgins PA, Burant CJ. Knowledge, Attitudes, and Predictors of Advance Directive Discussions of Registered Nurses. West J Nurs Res 2004;26:784–96.
- [28]. Cagle JG, Van Dussen DJ, Culler KL, Carrion I, Hong S, Guralnik J, et al. Knowledge About Hospice: Exploring Misconceptions, Attitudes, and Preferences for Care. Am J Hosp Palliat Care 2016;33:27–33.
- [29]. Grachinski Buiar P, Goldim JR. Barriers to the composition and implementation of advance directives in oncology: a literature review. ecancer 2019;13.
- [30]. Krakauer EL, Crenner C, Fox K. Barriers to Optimum End-of-life Care for Minority Patients. Journal of the American Geriatrics Society 2002;50:182–90.
- [31]. Saeed F, Xing G, Tancredi DJ, Epstein RM, Fiscella KA, Norton SA, et al. Is Annual Income a Predictor of Completion of Advance Directives (ADs) in Patients With Cancer. Am J Hosp Palliat Care 2019;36:402–7.
- [32]. Shen MJ, Prigerson HG, Paulk E, Trevino KM, Penedo FJ, Tergas AI, et al. Impact of end-of-life discussions on the reduction of Latino/non-Latino disparities in do-notresuscitate order completion: Latino Disparities and DNR Order Completion. Cancer 2016;122:1749–56.

- [33]. Huang IA, Neuhaus JM, Chiong W. Racial and Ethnic Differences in Advance Directive Possession: Role of Demographic Factors, Religious Affiliation, and Personal Health Values in a National Survey of Older Adults. Journal of Palliative Medicine 2016;19:149–56.
- [34]. LoPresti MA, Dement F, Gold HT. End-of-Life Care for People With Cancer From Ethnic Minority Groups: A Systematic Review. Am J Hosp Palliat Care 2016;33:291–305.
- [35]. McGlade C, Daly E, McCarthy J, Cornally N, Weathers E, O'Caoimh R, et al. Challenges in implementing an advance care planning programme in long-term care. Nurs Ethics 2017;24:87–99.
- [36]. Janssen DJA, Spruit MA, Schols JMGA, Cox B, Nawrot TS, Curtis JR, et al. Predicting Changes in Preferences for Life-Sustaining Treatment Among Patients With Advanced Chronic Organ Failure. Chest 2012;141:1251–9.
- [37]. Janssen DJA, Spruit MA, Schols JMGA, Wouters EFM. Dynamic Preferences for Site of Death Among Patients With Advanced Chronic Obstructive Pulmonary Disease, Chronic Heart Failure, or Chronic Renal Failure. Journal of Pain and Symptom Management 2013;46:826–36.
- [38]. Dixe M dos A, Santo ID de O, Lopes S, Catarino H, Duarte S, Querido A, et al. Knowledge and Myths about Palliative Care among the General Public and Health Care Professionals in Portugal. IJERPH 2020;17:4630.
- [39]. Sheehan DK, Schirm V. End-of-Life Care of Older Adults: Debunking some common misconceptions about dying in old age. AJN, American Journal of Nursing 2003;103:48–58.

Table 1. Validity of Chung et al (Retrospective Cohort)[9]
--

Question	Yes/No/ Unclear	Explanation
Was the assignment of patients to treatments randomized?	No	There is no randomization in this study since this study is a cohort retrospective study that compares the completion of AD before and after a bill concerning the suspension of end-of-life care was passed.
Were the groups similar at the start of the trial?	Yes	There is no significant difference between patient characteristics before and after the bill was passed with P-value > 0.05
Aside from the allocated treatment, were groups treated equally?	Yes	The study is a retrospective cohort with no direct intervention by the researcher.
Were all patients who entered the trial accounted for? And were they analyzed in the groups to which they were randomized?	Unclear	There is no randomization in this study but almost all patients were included in the analysis with 2 patients before the bill was passed and 3 patients after who were excluded because of incomplete medical records.
Were measures objective or were the patients and clinicians kept "blind" to which treatment was being received?	No	There is no blinding in this study since it's a retrospective cohort study.
Level of evidence	2b	

 Table 2. Validity of Courtright et al and Halpern et al (RCT)[10,11]

Question		Courtright et al	Halpern et al		
Was the assignment of patients to treatments randomized?	Yes	Randomization was done electronically with 50% probability to be included in each group.	Yes	Randomization was done electronically with 1 in 3 probability to be included in each group.	
Were the groups similar at the start of the trial?	Yes	There is no significant difference in baseline characteristics of the two groups except for the religion variable.	Unclear	There is baseline characteristics for each group but no statistical analysis to compare each variable.	
Aside from the allocated treatment, were groups treated equally?	Yes	The only intervention given was expanded choice set.	Yes	The only intervention given were standard or modified AD.	
Were all patients who entered the trial accounted for? And were they analyzed in the groups to which they were randomized?	No	127 of 160 (78.4%) patients in the standard choice group completed the 3 months follow-up and 129 of 156 (81.1%) patients in the expanded choice set group.	No	 85 of 175 (48.6%) patients in comfort AD group, 91 in 171 (53.2%) in standard AD group, and 88 of 169 (52.1%) in life-extending AD group die to a lot of patients not completing AD. 	
Were measures objective or were the patients and clinicians kept "blind" to which treatment was being received?	Yes	There is blinding for the research coordinator until the patients signed informed consent form and in the investigators who did the statistical analysis.	Yes	There is blinding for the research staff who contacted patients during the follow-up.	
Level of evidence	1b		1b		

Question		MacKenzie et al	Houben	et al
What question (PICO) did the systematic review address?	Yes	What is the effectiveness of Respecting Choices and related models on ACP outcomes?	Yes	What is the effectiveness of Advance Care Planning in the adult population?
Is it unlikely that important, relevant studies were missed?	Yes	Literature search was done in the PubMed, CINAHL, and Google Scholar databases and 745 articles was found after duplicates were removed.	Yes	Literature search was done in Medline/PubMed and Cochrane for articles published from 1966 to 2013 and 26628 articles were found and then filtered down to 56 articles.
Were the criteria used to select articles for inclusion appropriate?	Yes	Inclusion criteria in this study is the Respecting Choices protocol and other protocols that are adapted from Respecting Choices.	Yes	Inclusion criteria in this study is articles with original data, RCT study design, and written in English.
Were the included studies sufficiently valid for the type of question asked?	No	Articles selected for this systematic review were evaluated with the GRADE criteria, however a majority of the articles had high risk of bias.	Unclear	In the limitation section the author stated that 55.4% of the articles analyzed were low-quality RCT after being evaluated with PEDro score due to the lack of blinding.
Were the results similar from study to study?	Unclear	There is evidence for Respecting Choices increasing AD completion but unclear and variable evidence between AD and treatment concordance.	Yes	Heterogeneity test values were available for AD completion (τ^2 = 1,15; χ^2 = 60,63 P <0,00001; I ² =79%), end-of-life preferences (τ^2 = 0,21; χ^2 = 8,29 P= 0,04; I ² =64%), and concordance (τ^2 = 1,05; χ^2 = 7,60 P= 0,02; I ² =74%).
Level of evidence	1a, 3a	1a for AD completion, 3a for the concordance between AD and actual treatments patient received.	1a	

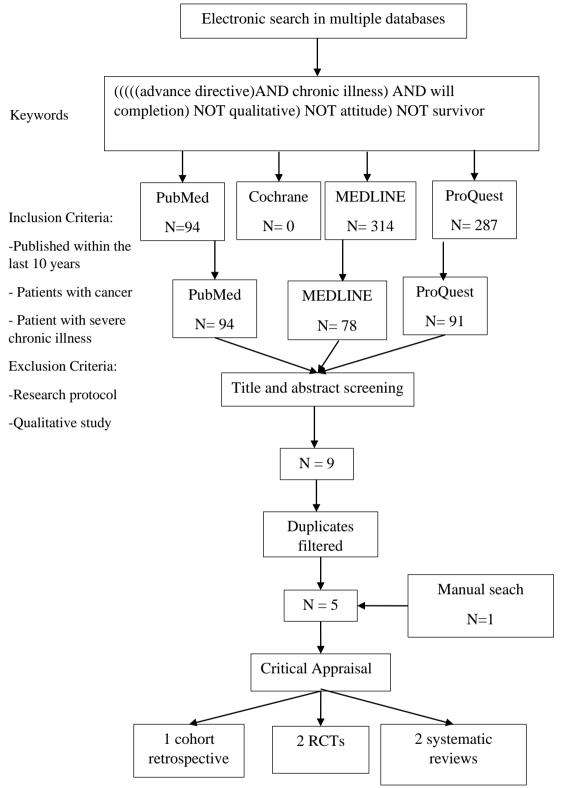


Fig. 1. Search strategy and screening process

Variable	Group				
	Orders for LST before enforcement of the LEMD law (n = 20)	Advance directives after enforcement of the LEMD law (n = 78)			
Length of stay in the ER (min)	510.5 (349.5, 1085)	970.5 (462, 1615)	0.042		
Length of hospital stay (days)	5.5 (3, 10)	2 (0, 10)	0.061		
Medical expenses (won)	3,593,733.5 (2,439,355.5, 4,899,793.5)	2,167,290.5 (961,601, 6,025,705)	0.133		
Type of ER visit			0.025		
Direct visit to the ER without transfer from another hospital	10 (50.0)	61 (78.2)			
Transfer from another hospital	10 (50.0)	16 (20.5)			
Transfer from the OPD	0 (0.0)	1 (1.3)			
Transfer from the ER to a secondary hospital	0 (0.0)	18 (23.1)	0.020		
Transfer from the ER to a nursing hospital	0 (0.0)	7 (9.1)	0.339		
Survival in the ER	18 (90.0)	74 (94.9)	0.599		
Life-sustaining treatments and life-sustaining procedures					
Consent to perform CPR	0 (0.0)	0 (0.0)			
Consent to perform intubation	1 (5.0)	5 (6.4)	> 0.999		
Consent to perform CRRT	0 (0.0)	4 (5.1)	0.579		
Consent for ICU admission	1 (5.0)	3 (3.9)	>0.999		
Survival at discharge	3 (15.0)	49 (62.8)	0.001		

Data are presented as the median (Q1, Q3) for continuous variables and number (%) for categorical variables

LST Life-Sustaining-treatment, CPR cardiopulmonary resuscitation, CRRT continuous renal replacement therapy, ICU intensive care unit, ER emergency room, OPD outpatient department

Figure 2. Comparison of variables before and after the enforcement of LEMD law[9]

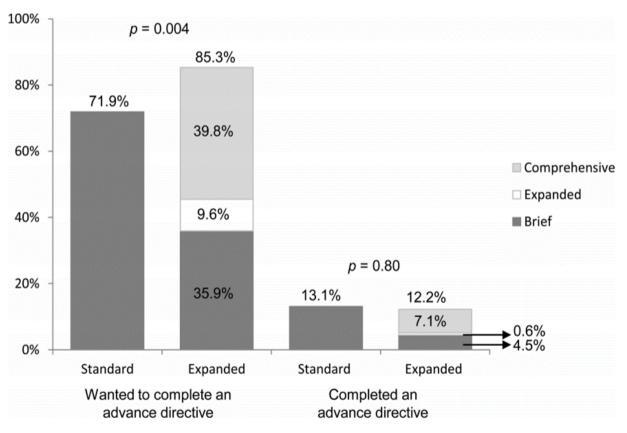


Figure 3. Percentage of patients who wanted to complete and completed an advance directive[10]

ISSN No:-2456-2165

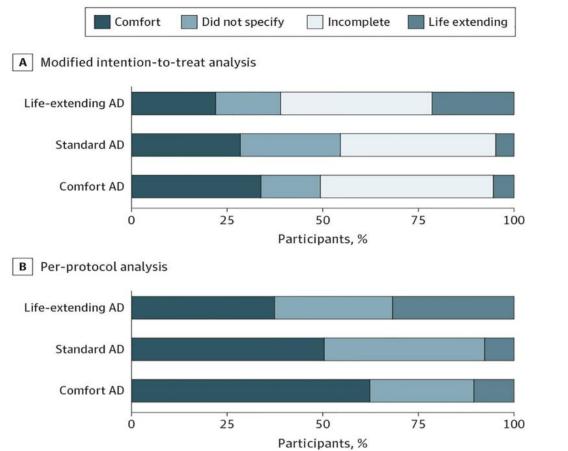


Figure 4. Percentage of AD made within each group in both modified intention-to-treat and per-protocol analysis[11]

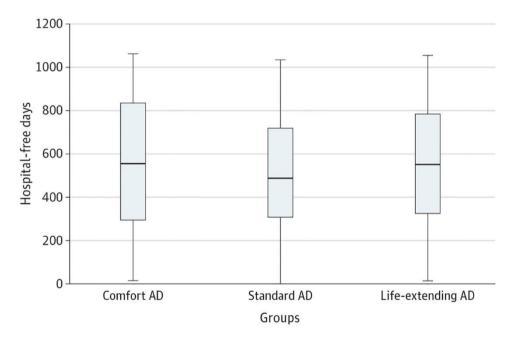


Figure 5. Comparison of hospital-free days for each group[11]

	Interver	ntion	Control			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
3.3.1 Intervention Ad	vance Dire	ectives	a service a				
Dexter 1998 (1)	17	219	8	253	6.5%	2.58 [1.09, 6.10]	
Dexter 1998 (2)	8	260	8	253	6.1%	0.97 [0.36, 2.63]	
Dexter 1998 (3)	70	277	8	253	6.8%	10.36 [4.87, 22.02]	
Heiman 2004 (1)	5	385	5	334	5.3%	0.87 [0.25, 3.02]	
Heiman 2004 (2)	38	360	5	334	6.2%	7.77 [3.02, 19.98]	
Landry 1997	36	95	22	92	7.2%	1.94 [1.03, 3.66]	→
Perry 2005 (1)	22	63	8	81	6.4%	4.90 [2.00, 11.98]	
Perry 2005 (2)	7	59	8	81	5.8%	1.23 [0.42, 3.60]	`_`
Richter 1995	18	87	1	89	3.4%	22.96 [2.99, 176.23]	
Rubin 1994	102	552	2	549	4.9%	61.99 [15.21, 252.65]	
Sachs 1992	1	52	3	85	2.9%	0.54 [0.05, 5.29]	
Sulmasy 1996 (1)	1	86	1	101	2.2%	1.18 [0.07, 19.09]	
Sulmasy 1996 (2)	0	63	1	101	1.8%	0.53 [0.02, 13.15]	
Walker 1999	11	39	3	35	5.0%	4.19 [1.06, 16.55]	
Subtotal (95% CI)		2597		2641	70.6%	3.31 [1.69, 6.50]	•
Total events	336		83				
Heterogeneity: t ² = 1.	15; X ² = 60	0.63, df	= 13 (P <	.0000	1); I ² = 79	%	
Test for overall effect	Z= 3.48 (P = .000	05)				
3.3.2 Intervention co	mmunicat	ion					
Gade 2008	66	275	34	237	7.6%	1.89 [1.19, 2.98]	
Grimaldo 2001	16	97	2	98	4.6%	9.48 [2.12, 42.47]	
Heffner 2001	8	99	15	185	6.4%	1.00 [0.41, 2.44]	
Nicolasora 2006	13	136	1	161	3.4%	16.91 [2.18, 131.03]	
Pearlman 2005	57	119	30	129	7.4%	3.03 [1.76, 5.23]	
Subtotal (95% CI)		726		810	29.4%	2.76 [1.41, 5.37]	-
Total events	160		82				1222
Heterogeneity: $\tau^a = 0$.	34; X ² = 12	2.40, df	= 4 (P = .	01); 🖻 =	: 68%		
Test for overall effect	Z=2.98 (P = .003	3)				
Total (95% CI)		3323		3451	100.0%	3.26 [2.00, 5.32]	•
Total events	496		165				
Heterogeneity: $\tau^a = 0$.	77; X= 78	6.50, df	= 18 (P +	.00001	1); I ² = 76	%	0.01 0.1 1 10 10
Test for overall effect	7 = 4730	P < 000	1011				Favours [control] Favours [interventi

Figure 6. Meta-analysis for AD completion outcome

	Interven	ntion	Contr	lo		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.2.1 Intervention Ad	vance Dire	ectives					
Dexter 1998 (1)	33	219	11	253	9.4%	3.90 [1.92, 7.93]	
Dexter 1998 (2)	26	260	11	253	9.1%	2.44 [1.18, 5.06]	
Dexter 1998 (3)	67	277	11	253	10.0%	7.02 [3.61, 13.63]	
Landry 1997 Subtotal (95% CI)	69	95 851	52	92 851	10.8% 39.4%	2.04 [1.11, 3.76] 3.41 [1.94, 5.98]	
Total events	195		85				-
Heterogeneity: $\tau^{a} = 0$. Test for overall effect				4); l ^a =	64%		
2.2.2 Intervention co	mmunicat	ion					
Au 2012	117	194	56	182	14.2%	3.42 [2.23, 5.24]	-
Clayton 2007	27	90	8	80	7.5%	3.86 [1.63, 9.10]	
Heffner 2001	18	99	24	185	10.0%	1.49 [0.77, 2.90]	+
Jacobsen 2011	175	517	81	382	16.5%	1.90 [1.40, 2.58]	+
Pearlman 2005 Subtotal (95% CI)	76	119 1019	49	129 958	12.5% 60.6%	2.89 [1.72, 4.83] 2.48 [1.78, 3.44]	↓
Total events	413		218				
Test for overall effect Total (95% CI)	Z = 5.39 (P < .000)01)	1809	100.0%	2.82 [2.09, 3.79]	•
Total events	608		303				· ·
Heterogeneity: τ [#] = 0. Test for overall effect Test for subgroup dif	Z= 6.82 (/	P < .000 Chi# = 0	001) .92, df = 1	1 (P = .)	34), I* = 0		0.01 0.1 1 10 10 Favours [control] Favours [intervent
C Effect of inte	erventio	ns vs					
C Effect of inte	erventio			e and	the e	nd-of-life care re	Ceiveu
	Interven	of-li ntion	ife car	ol		nd-of-life care re Odds Ratio	Odds Ratio
Study or Subgroup	Interven Events	of-li ntion Total	Contr Events	ol Total	Weight	nd-of-life care re Odds Ratio M-H, Random, 95% CI	
Study or Subgroup Detering 2010	Interven Events 25	of-li ntion Total 29	ife care Contr Events 8	ol Total 27	Weight 31.6%	nd-of-life care re Odds Ratio M-H, Random, 95% CI 14.84 [3.89, 56.71]	Odds Ratio
Study or Subgroup Detering 2010 Kirchhoff 2012	Interven Events 25 46	of-li ntion Total 29 62	ife car Contr Events 8 30	Total 27 48	Weight 31.6% 39.2%	nd-of-life care re- Odds Ratio M-H, Random, 95% CI 14.84 [3.89, 56.71] 1.73 [0.76, 3.90]	Odds Ratio
Study or Subgroup Detering 2010 Kirchhoff 2012	Interven Events 25	of-li ntion Total 29	ife care Contr Events 8	ol Total 27	Weight 31.6%	nd-of-life care re Odds Ratio M-H, Random, 95% CI 14.84 [3.89, 56.71]	Odds Ratio
Study or Subgroup Detering 2010 Kirchhoff 2012 Morrison 2005 Total (95% CI)	Interven Events 25 46 47	of-li ntion Total 29 62	ife car Contr Events 8 30 79	rol Total 27 48 96	Weight 31.6% 39.2%	nd-of-life care re- Odds Ratio M-H, Random, 95% CI 14.84 [3.89, 56.71] 1.73 [0.76, 3.90]	Odds Ratio
Study or Subgroup Detering 2010 Kirchhoff 2012 Morrison 2005	Interven Events 25 46 47 118	of-li ntion 70tal 29 62 49 140	fe car Contr Events 8 30 79 117	ol Total 27 48 96 171	Weight 31.6% 39.2% 29.2% 100.0%	nd-of-life care ree Odds Ratio M-H, Random, 95% CI 14.84 [3.89, 56.71] 1.73 [0.76, 3.90] 5.06 [1.12, 22.87]	Odds Ratio

Figure 7. Meta-analysis for the occurrence of end-of-life discussion and concordance of AD and end-of-life care received