

EFFECTIVENESS OF A BRIEF INFORMATION ABOUT ADVANCE DIRECTIVES IN PRIMARY CARE: A RANDOMIZED CLINICAL TRIAL

Promoter of the study: Proposal of own initiative of the researcher Yolanda Rando Matos to present as thesis of the Master's Degree Design and Analysis of Clinical Investigations of the Official College of Physicians of Barcelona (COMB) of the thesis student Yolanda Rando Matos.

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Study to be presented in the design phase to the Master of the COMB.

ABSTRACT

The knowledge and completion of advance directives (ADs) by the population is generally low. Primary care could develop a very important role to inform and assist in the preparation of this document because of its accessibility.

Objective: To evaluate the effectiveness of an oral brief information and a brochure administered in primary care to improve the proportion of ADs records.

Design: Randomized clinical trial.

Ambit: 7 offices from a urban health center in Hospitalet de Llobregat which serves about 25,000 users older than 18 years.

Material and methods

It will be administered randomly triptych and oral brief information about the existence of advance directives for people over 18 to attend the appointment of their family doctor for any reason (intervention group). It will be given the possibility of more extensive information if they wish and collaboration will be offered for the advance directive according to patient preferences. The control group will not receive any information. Follow-up: 3 months. Variables will be: number of people interested in ADs, number of ADs made and demographic data (gender, age, education level, race, comorbidities, religion, testament) in both groups. Statistical analysis: multiple linear regression, Poisson and Cox as response analyzed, with the intervention/control group as the main variable adjusting for potential confounders. Bivariate comparison using Student t test or Mann-Whitney test (continuous variables) and chi-square or Fisher's exact test (categorical variables). 165 subjects were required in the control group and 165 in the intervention group.

Conclusion: positive results of this study will bring out the brief information managed by family physicians increases the number of ADs thus facilitating the right to autonomy of the patient.

Keywords: Primary care, Advance directives, Randomized clinical trial.

INTRODUCTION

The development of biomedical science has managed to improve the quality of life of patients as well as increase their life expectancy. However, the therapeutic bane that is sometimes performed at the end of the patient's life by health professionals has motivated legislation on the extent of therapeutic measures that prolong life unnecessarily, that is, when there is no improvement quality of life. The concept of therapeutic effort limitation has emerged in recent years in relation to these ethical problems (1,2).

The paternalistic model of the physician is increasingly relegated to the biopsychosocial or patient-centered model, where his preferences, beliefs and expectations are taken into account. Unfortunately, we can find situations where the patient can not express his choice in the face of aggressive treatment, for example in case of severe cognitive impairment or a decrease in non-reversible level of consciousness. These situations raise doubts and fears to relatives and health professionals about what the patient would have preferred had he or she manifested. For these reasons, in parallel with the progress of technology in medicine, legal attempts are being made to improve the rights of patients regarding their autonomy to decide on their health.

Historical landmark

The first vital wills were proposed in the United States in the mid-1960s following the meeting of the Euthanasia Society of America. The document was defined as "testament" whereby the patient could express the way he wanted to be treated if he could not decide for himself (3). But it was only after 1976, in the state of California, that they became legal. These documents already rejected vital support measures when there were no expectations of recovery and requested measures of care and treatment of pain. However, problems arose when knowing who should interpret the wishes of the patient, hence the figure of the representative appointed by the patient. Another problem was the scarce diffusion of the document due to barriers on the part of the sanitarians (discomfort to talk about the subject) and of the population (belief that it was only for the elderly or the chronically ill) (4). In the 1990s, attempts were made to overcome these barriers through meetings of experts and large-scale studies (5,6).

Descriptive data of the different studies

Studies describing the baseline characteristics of patients who formalize an advance directive document (DVA) provide figures for gender and educational level. Thus, women are twice as likely to perform the document than men in 2 Spanish studies (7,8) and the secondary or higher education level has been related to a higher proportion of document completion (9,10).

Other factors described in literature with a strong association with completing a VAD are having a religious denomination (9,11), having a relative with the document (odds ratio -OR - 17.3) (9), a long relationship with the general practitioner (OR 3.5) (9), having a larger number of children and being widowed (11).

In a study of 3055 households in South Australia, it was observed that low social classes and people who have not made financial wills are less likely to complete the VAD (10).

There are cultural differences between the North and the South of Europe regarding concepts related to the end of life. According to a study carried out in Spain, Italy and Portugal, in these countries, more importance is given to religion, to being able to die at home and to family ties (12,13).

Clinical trials to increase DVA registration

A meta-analysis of the studies published between 2000 and 2012 to assess the effects of anticipated changes in care at the end of life showed that most of them are performed in a hospital setting or nursing homes (14).

A systematic review of 2008 that evaluated the effectiveness of different interventions to promote early will in the elderly showed that most studies conducted a single educational session and measured outcomes over the next 6 months. The mean OR calculated for the performance of the document in the intervention groups was 2.6 (15). In another similar systematic review but whose population was non-terminal patients, it was observed that the majority of studies were of low quality and in the most rigorous the OR was 2.42 for different educational interventions (written materials, videos or audios) .

Different ways of increasing the realization of DVA have been studied: written material only, written material with a single educational session or written material, and educational sessions. In a review of the the literature of 2007 concluded that only the multifaceted modalities increased the interest of the patients to talk about the subject with their doctors.

Tamayo et al. also observed in another systematic review that the best intervention to increase the proportions of DVA is the combination of informational material and repeated conversations in clinical visits (18).

Studies carried out in Primary Care

It is striking the good acceptance by the population towards the DVA and the scarce record of it. Angora et al., In a study in which patients aged over 65 years were interviewed in a primary care center, found that the patients were in agreement with the possibility of performing the document despite the underutilization of this resource (19). Santos et al., Also through primary care surveys, found that 97% considered it interesting, 39% said they would, and 86% did not feel uncomfortable talking to their family doctor (20). Similar results were obtained by Llordés et al. in corroborating that there was little information and much interest in this process (21).

The citizens' assessment of the possibility of making a document of advance directives is very positive, but only 1.9% in Catalonia and 0.5% in Andalusia of the respondents had done it (22,23). In Andalusia, it was also seen the importance of the information leaflet in the health center to increase satisfaction. (23)

Regarding intervention studies to increase the records of DVA performed in Primary Care, we have that of Donahue et al. who obtained a 32.5% increase in VAD by mailing the information prior to the arranged visit with their family doctor and completing it in successive visits in a period of 3 months (24).

Wisow et al., In a quasi-experimental study of 1 year duration, promoted the anticipated will in over 65 in health centers through oral and written education (a letter prior to a control visit and a subsequent reminder visit) administered by

family doctors and used another health center as a control. The result was an increase of 7'8% of registrations with respect to <1% in the control center (25). According to another study in Primary Care (Ramsaroop, 2007), the information leaflet alone is not effective and the best would be multiple educational visits to promote the attitude change phase towards the ADs procedure (26).

Hypothesis of the study

Giving brief oral and written information to patients visited by your family doctor on a prior appointment increases the proportion of DVA records by 8%.

Providing a brief oral and written information to patients visited by their family doctor in a previous appointment increases the proportion of people interested in this right (there is no previous bibliography on this data).

People who write a DVT are usually older, white, women, have more children, have a will and have more comorbidity than those who do not.

MAIN OBJECTIVE

To evaluate the effect of brief oral and written information on the advance directive document (DVA) administered by primary care physicians, compared to usual clinical practice, on the proportion of persons interested in or performing the VAD in 3 months in the adult population (over 18 years old) who attend a Primary Care appointment.

SECONDARY OBJECTIVES

Evaluate the baseline characteristics of those who perform or are interested in VAD (whether they are in the control or intervention group).

To assess the baseline characteristics of those performing the DVA and those not within the intervention group.

Evaluate the reasons why patients finally formalize the document by open question (will be categorized if there is a limited number of responses, otherwise the reasons will be described qualitatively).

Evaluate the average time to perform the DVA from the day of the patient's recruitment.

MATERIAL AND METHODS

Design

Parallel group unicentric randomized clinical trial. Prospective primary care intervention study.

For randomization, randomly generated numbers will be used in closed envelopes controlled by a professional outside the study. Subsequent masking is not appropriate for the patient. The randomization unit will be the patient.

Sample

Open-label (or non-blind) unicentric randomized clinical trial of parallel groups. Simple random sample of patients who go to an appointment with their family doctor.

Inclusion criteria: Patients older than 18 years old who go to their family doctor by appointment.

Exclusion criteria:

- Patients with language barrier
- Patients younger than 18 years (AD not provided for by law) (28)
- Patients with altered decision-making ability according to computerized clinical history by coding in health problems or mentioned in a clinical course of computerized medical history (eCAP): cognitive impairment, dementia, mental retardation diagnosed. Although there are studies on attitudes towards ADs of people with early cognitive impairment (Minimental > 18), it was decided to discard because the intervention should be brief. The cited study also concludes that this type of patients prefer to delegate decisions to the family. (29)
- Patients who come spontaneously to their family doctor.
- Patients who have already been recruited previously in the study. Patients who may visit by appointment only on more than one occasion will only participate once and subsequent visits for recruitment will be excluded. In addition, there will be no reinforcement of the study intervention in these visits.
- Patients who have already formalized the ADs.
- Patients who do not wish to participate in the study.

Calculation of sample size: In order to know the magnitude of the effect of similar studies in primary care with similar interventions (written and oral information vs no intervention), the Wissow study (25) was chosen, where the proportion of VAD obtained in intervention group was 7.8% vs. <1% in the placebo group.

In calculating proportions in cohort studies or clinical trials:

Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a bilateral contrast, 165 individuals in the intervention group and 165 in the control group are required to detect a minimum relative risk of 7.8 ($= 7.8\% / 1\%$) taking the rate of VAD in the intervention group as 7.8% and in the control group of 1%. A rate of loss has been estimated for refusing the 10% share. The POISSON approximation has been used in the statistical calculator GRANMO, version 7.12 online (Program of Research in Inflammatory and Cardiovascular Disorders, Institut Municipal de Investigació Mèdica, Barcelona, Spain)

Although hypothetically no losses are expected, they may have been relinquished to participate for different reasons. In order to avoid a selection bias produced by the relationship of giving up with the fact of wanting to do a VAD, patients refusing to participate will be excluded and the motive, age and sex will be collected to compare if there are differences between the two groups regarding these characteristics.

Ambit

Florida Nord de l'Hospitalet de Llobregat Primary Care Center, an urban area with a population of approximately 25,000 people. Multicultural neighborhood with low socioeconomic status. The follow-up time for the intervention will be 3 months.

Information sources

Records of shared clinical history in eCAP. Patient questions about independent variables if they are not recorded.

Recruitment procedure

Consecutive recruitment: They will be consecutively obtained from different quotas (both afternoon shift and morning shift) so that the sample is representative of the study population.

Participate the quotas of the center whose doctor in charge has wanted to participate in the study. In order to avoid a selection bias and a more active doctor than another to have more patients represented in the study, a mechanism will be established whereby everyone will have the same probability of recruiting a similar number: the first 6 visits of each day for 8 days. The recruitment period will be made from 01/06/2015 to 09/30/2015, until the sample is completed. The follow-up period will be 3 months for each patient (both intervention and control).

A list of random numbers will be created and divided among the 7 consultations of the participating physicians in the study. Each day, the first 6 visits to the list will be recruited for 8 days prior appointment or until the sample is completed.

Patients will be randomized according to the list of random numbers guarded by a professional (or several) other than the study that will be located in the adjacent consultation. In case there is no professional close, the list will be delivered with a

closed envelope to another professional and will be contacted by telephone. Patients will be treated with the intervention when the number is 1 and control if it is 0. This number will be asked prior to the patient's entry into the consultation.

Predictive or independent variables to be obtained at the time of the first visit

For stratified analysis.

- Sex: Male, Female
- Race: Caucasian vs non-Caucasian
- Age in years
- Level studies: Primary, secondary, university, without studies.
- Comorbidity: measured by the Charlson index. Score: a) 0-1: no comorbidity; b) 2: low comorbidity; c) ≥ 3 : high comorbidity. (Charlson.webloc calculator).
- Testament on material goods: Yes, no.
- Religious Confession: yes, no. Is considered a practitioner: yes, no
- Marital status: single, married, widowed, separated / divorced
- Number of children

To obtain this information will be extracted from the computerized medical history or the patient will be asked.

Intervention

Patients who are included in the intervention group, if they meet the inclusion criteria and do not present any exclusion criteria, will be given brief information about the existence of the document of anticipated wills after resolving the reason for the visit for which they had come the patient. This information will not last more than 3 minutes and will not be repeated on successive visits within the recruitment period. Also, an informative triptych (see attachments) will be given to the patient so that he can read it at home. These leaflets have been made by the Department of Health of the Generalitat de Catalunya. They will be advised that we can extend the information if they are interested or help them to do the document in the near future if they want, we will inform you that we would wait for the answer before 3 months (24). In case of interest, you can leave your information in the User Service of the outpatient clinic by specifying name, telephone number and reference doctor or ask for an appointment again.

Patients who fall into a control group will only be attended to their reason for visiting and will be asked for the necessary data to obtain the independent variables if they do not appear in their history. If the patient in this group wants the information, he will be excluded from the study because he "refuses to participate."

If the patient, both the control group and the intervention group, has some exclusion criteria, it will be recorded as a screening failure and their randomization number will not be re-used for the next patient.

All patient information will be kept confidential.

Result or dependent variables

They will be obtained at the moment that the patient shows interest in the intervention, or else, by asking by appointment or by telephone within 3 months of their recruitment:

- Interest in information about DVA: yes, no. Number of patients who have come to their family doctor (MF) to request information or have been interested by telephone in each group.
- Implementation of DVA: yes, no. Number of patients in each group.

In case of not being able to contact the telephone patient or face to face at 3 months, the DVA registration will be viewed at the Primary Care Clinic Station (eCAP), which is the computerized medical history program used by all professionals in the network of primary care of the Institut Català de la Salut (ICS). The document can be accessed from:

- HC3 - Notices: shared clinical history projects in Catalonia.
 - Dades del pacient: Documents of anticipated voluntats
- Registration from the Department of Health is autonomous, although not done in the ABS. From other institutions, the patient is always advised to take the DVA to his health center.
- Open question to know the reason that has led to formalize the DVA, both to patients in the intervention group and control.
 - Time to perform the DVA from the day of recruitment, expressed in days, to both the intervention and control patients.

Limitations and ethical considerations

- Possible increase in response in the intervention group due to the link with the family physician (participation bias). It could be wrongly concluded that the intervention is effective when compared to the control group. Randomization of the sample is intended to partially avoid this problem.
- Possible contamination of the groups when living in the same neighborhood and the possibility of communication between the patients in the control group and the intervention group. To find out this, patients in the control group will be asked to become interested or to do DVA if they have been informed by other patients of the study through the questions: Do you know anyone else who participates in this study? Did you talk about the study with that person?
- Bias of hyper-attendees: they are more likely to be chosen for the study however this problem is within usual clinical practice. The information will not be repeated to the patient who has already been randomized.

The study has been submitted to the Ethical Committee for Clinical Research (CEIC) of the University Institute for Research in Primary Care (IDIAP) Jordi Gol, and is awaiting the results of its evaluation. When accessing the eCAP and / or performing a personal interview to complete information on the variables is required, the patient's signed informed consent will be requested through his physician. The confidentiality of the subjects included in the study will be

guaranteed according to the Organic Law on Protection of Personal Data (15/1999 of December 13, LOPD). Researchers are committed to maintaining the confidentiality of information, working with anonymous patient data, and respecting current ethical and research practice standards.

Statistical Analysis Plan (SAP)

Intention-to-treat analysis. No intermediate analysis is planned. A bilateral significance level of 5%, 95% CI and 80% power will be used. The SPSS V21 program will be used. Analysis of efficacy of unadjusted parallel clinical trials. Data will be analyzed according to the CONSORT guidance and comparisons between groups will be based on the intention-to-treat principle. First: analysis of the baseline comparability of the study groups in relation to the variables studied. Descriptive statistics of all variables collected. The Student's t test or the Mann-Whitney U test (according to the frequency distribution of the variables studied) will be used to compare continuous variables, and Chi-square or Fisher's exact test for comparison of categorical variables.

In the case of finding a very different distribution of the independent baseline variables (1st visit) between the two groups, which would indicate an obvious selection bias despite randomization, the possibility of analyzing as a cohort study by means of propensity score techniques .

- Main objective "To assess the effect of brief oral and written information on the Advance Directives (ADs) given by primary care physicians, compared to usual clinical practice, on the proportion of persons interested in or performing VAD in 3 months in a heterogeneous group of patients (different ages and ethnicities) who go to a previous appointment ": inferential analysis of effectiveness, analysis of proportions of two samples. A multivariate logistic regression analysis with the variables of interest or realization of the yes / no VAS as the dependent variable will be performed and the group assigned as an independent variable, adjusting for the potential confounding factors.

- Secondary objectives: demographic and clinical characteristics that are considered likely to be associated with the completion of a priori VAD or that differ between study groups will be included in the logistic regression model for the dichotomous dependent variable.

1 · "Evaluate the baseline characteristics of those who perform or are interested in the VAD of both the control group and the intervention group": descriptive analysis for independent quantitative variables (age, number of children) and for qualitative variables , studies, comorbidity, religion, testament, marital status), frequency tables. Bivariate analysis using as a dependent variable the answer yes or no to the realization of the DVA or interest by DVA and as independent variables the basal characteristics. The Student's t test or the Mann-Whitney U test (according to the frequency distribution of the variables studied) will be used to compare continuous variables, and Chi-square or Fisher's exact test for comparison of categorical variables.

2 · "Evaluate the baseline characteristics of those who perform the VAD and those who are not in the intervention group": descriptive analysis for independent quantitative variables (age, number of children) and for qualitative variables (gender, race, comorbidity, religion, testament, marital status), frequency tables.

Bivariate analysis using as a dependent variable the answer yes or no to the realization of the VAD within the intervention group and as independent variables the basal characteristics. The Student's t test or the Mann-Whitney U test (according to the frequency distribution of the variables studied) will be used to compare continuous variables, and Chi-square or Fisher's exact test for comparison of categorical variables.

3 · "Evaluate the reasons why the document is formalized by open question": it will be categorized if there is a limited number of categories of responses and a descriptive univariate analysis will be done (frequency tables). In case of multiple answers the reasons will be described qualitatively.

4 · "Evaluate the average time to perform the DVA from the day of recruitment of the patient.": Univariate descriptive analysis.

SCHEDULE OF ACTIVITIES

- o Implementation of the protocol: From October 2014 to May 2015. Directed by Antoni Vives, Noemi Moreno and Yolanda Rando.
- o Ethical committee approval and health authorities: will be sent to USR Metropolitana Nord (Jesús Almeda): April –June 2015. The shipment will be made by Yolanda Rando.
- o Recycling in advance wishes of the researcher: 2 sessions of 1 hour given by the lecturer: 2 days of May 2016.
- o Inclusion of the first and last patient: From 1 to 30 September 2016. Conducted by participating physicians: Toni Vives, Noemí Moreno, Estrella Rodero, Rosa M. Sorando, Raquel Adroer Martori, José Luis Ballvé, Yolanda Rando.
- o Completion of the last patient follow-up: From 1 to 30 December 2017. Conducted by participating physicians: Toni Vives, Noemí Moreno, Estrella Rodero, Rosa M. Sorando, José Luis Ballvé, Raquel Adroer Martori , Yolanda Rando.
- o Availability of results report: January-February 2017. Directed by Yolanda Rando
- o Plan validation data: March 2017. Directed by Yolanda Rando

NECESSARY RESOURCES

The study will be carried out at the Florida Nord EAP of L'Hospitalet de Llobregat, which has a long history as a teaching center attached to the Unitat Docent Multidisciplinary Family Medicine and Community of Ponent Coast.

Some of the researchers are tutors of this teaching unit.

The Florida Nord EAP has a computerized medical history since 2005.

We have the consultations, the computer resources and clinical tool consumable or inventoried necessary for the realization of the study. All visits and subpoeas will be in charge of the research team.

- o Paper or electronic data collection questionnaires
- o Informative triptychs on paper
- or Google drive to share documents and bibliography.
- o Clinical Data Manager: SPSS v 21 mac statistical package.
- o Medical personnel participating in the study: 7 family physicians
- or Nurse who keeps the list of random numbers (outside the study): 6 nurses
- o Administrative staff of the outpatient clinic for the introduction of the DVA in the computerized medical records: 2 administrative

IMPACT OF THE PROPOSED INVESTIGATION

This research aims to improve the patient's quality of life by reporting on a right that is often underused and that has repercussions on respect for autonomy. It would avoid unnecessary referrals to the hospital, performing complementary tests, applying invasive techniques and unnecessary prolongations of life if that was the patient's decision and was documented. It will bring benefits to the community, both at the level of patients and professionals, allowing the latter to have no uncertainties in the specific situations contemplated by the DVA.

The results of this study can be extrapolated to other communities and can transfer the knowledge generated by updating new guidelines and protocols of action in Primary Care.

In addition, new data will be obtained on a type of little-used intervention that will affect the expansion of the scientific literature.

EXPERIENCE AND CAPACITY OF THE RESEARCH GROUP SUBMITTING THE PROPOSAL

Tesinanda Yolanda Rando Matos: Adjunct physician at the center. She is an expert in the incorporation of new technologies into the clinical practice of primary care, being a reference of her center for diagnostic techniques such as the use of the non-mydratic chamber and therapeutics such as cryotherapy. She has collaborated in multicenter clinical trials as an associate researcher. He has attended several editions of the Conference of the ethics group of CAMFiC.

Antoni Vives Argilagós: Adjunct physician and teaching coordinator of the Center since its opening. Extensive experience as a tutor, both undergraduate and postgraduate. Experience in research in general focused mainly in the cardiovascular area, in implementation of new teaching techniques and specifically in the approach of ethical problems with the doctors in formation. He has attended several editions of the Conference of the ethics group of CAMFiC. He has collaborated in multicenter clinical trials as an associate researcher.

Noemi Moreno Farrés: Adjunct physician at the center. Experience as tutor, both undergraduate and postgraduate. It is referent of the center in respiratory pathology. She has collaborated in multicenter clinical trials as an associate researcher. He has attended several editions of the Conference of the ethics group of CAMFiC

Estrella Roderó Pérez: Adjunct physician at the center. She is expert in the control of the processes of Disability, temporary, being a reference of its center for techniques and therapeutics such as Infiltrations of locomotive apparatus and ambulatory minor surgery techniques. She has collaborated in multicenter clinical trials as an associate researcher. He has attended several editions of the Conference of the ethics group of CAMFiC.

Rosa M^a Sorando Alastruey: Adjunct physician at the center. She is an expert in the incorporation of therapeutic techniques into the clinical practice of Primary Care as the infiltrations of the locomotor system. She has collaborated in multicenter clinical trials as an associate researcher. He has attended several editions of the ICS Symposium.

Raquel Adroer Martori: Adjunct doctor of the center. Extensive experience as a tutor, both undergraduate and postgraduate. Experience in research in general focused mainly on the cardiovascular area.). He has attended several editions of the ICS Symposium. He has collaborated in multicenter clinical trials as an associate researcher.

José Luis Ballvé Moreno: is a member of the Accredited Research Group on Lifestyles of the IDIAP Primary Care Research Institute Jordi Gol. It has helped to translate the results of clinical research into the daily practice of primary care as Co-author of the "Guide for the detection and treatment of tabac consumption" (Guia Salut), researcher of ISTAPS study and as teacher in workshops and courses for smoker care. In 2009 he participated as a teacher in the course of urgent pathologies in primary care. He has collaborated in multicenter clinical trials as an associate researcher, currently a principal investigator of a multicenter clinical trial.

ANNEXES

Annex 1: Triptych DVA Spanish

Annex 2: Triptych DVA Catalan

Annex 3: Patient information sheet in Spanish

Annex 4: Patient information sheet in Catalan

Annex 5: Informed Consent in Spanish

Annex 6: Informed Consent in Catalan

Annexes 1 to 6 in separate document.

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