APPENDIX

**Table 1: Cohort studies assessment for validity**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***Article*** | ***Bias due to confounding*** | ***Bias in selection of participants*** | ***Bias in classification of interventions*** | ***Bias due to deviation from intended interventions*** | ***Bias due to missing data*** | ***Bias in measurement of outcome*** | ***Bias in selection of the reported results*** | ***overall bias*** | ***Summary*** |
| O’Mahony et al., 2010 (Before and after) | XXX Time in ICU is probably correlated to DNR | X Unlikely that intervention affected referral pattern | XPossibly PC given also before intervention, minimizing its effect.  | XXXXBefore- after study so co interventions likely | XIf indeed consecutive patients- no loss of data | XX Unblinded measurement in before-after design | x Non-significant data are reported | XXXHigh risk -non comparative study, and unblinded measurements | Very high risk |
| O’Mahony et al., 2010 (Case control) | XXXXPossibly differential characteristics in intervention campus Vs other campus | XXXX Possible selective referral to intervention campus. | X Probably not. If exists - minimizes the effect | X Palliative care supplied also at control campus (minimizing the effect) | X | X | XXX Only few outcomes of this sub study reported | XXXXVery high risk of bias- small samples, selection bias: included only those who died, differential characteristics not reported, called "case control" despite retrospective cohort (exposure Vs non-exposure) design | High risk |
| Tan et al., 2014 | XXX More comorbidities and more malignancies in 2010. possible other variables have changed over 3 years. | XXX Included only those who died, correlated to both PC and DNR | X | X | X | XX Non blinded measurement both of physicians and of researchers | X | XXXHigh risk due to before-after design, selection bias to those who died, significant co intervention and non-blinded measurements | High risk |
| Kao et al., 2014 | XXXCase control design raises risk of bias of multiple confounders. Example: sicker patients in the ACP group.  | XX Case- control design | X Presence of DNR status in medical file is a clear measurement | XXX Probably yes, many patient treatments correlated to both PC and DNR eg lack of curative treatment. | X Loss to follow up is small relative to the large sample size of 3156 patients | X | X | XXXHigh risk of bias- case control design, controlled for only some confounders, other important variables not included in multivariable analysis. | High risk |
| Ferrell et al., 2015 | XX Although before-after study is prone to bias, time periods were close, and study was explicitly designed to minimize bias. | XX Possibly patients that agreed to participate in the intervention were more prone to endorse ACP recommendations.  | X Very clear times | X Some control patients received PC, and possibly received PC even before study. Minimizing intervention effect | X Very good follow up | XX Non-blinded assessment. Time frame for collection of data well defined.  | X | XXAlthough co-intervention might affect outcome due to before- after design, groups were similar regarding confounders | Moderate risk |
| Bailey et al., 2014 | XXXNo adjustment to disease and treatment factors | XX Possible that patients were referred to research hospitals due to the intervention itself | X Probably not, though possible that patients moved from one hospital to another | X  | X | X Moderate risk of small bias, favoring intervention due to non-blinding of the research nurse collecting data from files | X | XXX High risk of bias due to confounding: readiness of hospitals, possible differential referral to hospitals, and measurement only of people who died, and researcher not blinded | High risk |
| Lustbader et al., 2011 | XXX Study population consisted of two retrospective cohorts. There is almost no information about the two groups. | XXX Comparison of patients from 2003-2004 to patients from 2005-2009, APACHE III scores were significantly higher for the control group. Selection of only people who died favors intervention since dying is related both to PC and to DNR  | X Patients in the control group possibly received PC and vice versa, minimizing effect | XX Historical cohort so possible co interventions that appeared during time. | XXXX Very high risk of bias, selection of only people who died, (related to both intervention and outcome) | XX Method of measurement is not reported, so non-blinding possible.  | X | XXXX Very high risk of bias: No control for confounders, missing data for those that did not die, co intervention in historical cohort design | Very high risk |
| Kerr et al., 2014 | XXXXPatients' medical condition confounds the effect of PC on AD completion | XXXOnly patients referred to PC included | XLow risk of bias, all people received the care | Non-relevant | XXX 186 of 685 (those still belonging to PC) excluded. | XX Partial description. possibly blinded since used computerized measuring | X | XXXX Very high risk of bias due to non-comparative study confounding and selection | Very high risk |
| Sacco, DeravinCarr and Viola, 2013 | XX Possibly the time in which PC consultation was done confounded association. | X PC was given to all (all patients referred) | X On admission some already had AD, minimizing the effect of PC. | XX Moderate risk- possibly other intervention during time | XXXNumbers of excluded not reported. Possibly excluded those with less information which may be those with less AD. | XX Documentation of DNR was part of the PC intervention | XX Statistical methods was not reported | XXXHigh risk- non-comparative cohort. Time confounding. Patient condition confounding | High risk |
| Rabow et al., 2004 | XXXGroups differed by primary care provider, possibly a confounding factor.  | XXXGroup assignment could have differed by patient preference.  | XClinics well defined and separated.  | XXXPossibly other co interventions in intervention group including different clinicians attitude and non blinding | XXXFifteen intervention patients (30%) and 9 controls (23%) did not complete the intervention | XXData was extracted from medical record, which was filled by intervention clinicians | XNon significant outcomes are reported | XXXConfounders and co-interventions by primary care providers and patient preferences.  | Very high risk.  |

**Low** **risk of bias-X**

**Moderate risk of bias-XX**

**High risk of bias-XXX**

 **XXXX- Critical risk of bias**

**Table 2: Randomized controlled trials (RCT) assessment for validity.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ***Article*** | ***Adequate sequence generation*** | ***Allocation concealment used*** | ***Blinding of participant*** | ***Incomplete outcome date*** | ***Selective outcome reporting*** | ***Other source of bias*** | ***consensus*** |
| Temel *et al.*, 2010 | V | NANot fully described | X Non-blinded RCT | X  A large percentage of patients did not complete follow up, and results are available only for a fraction of randomized patients. | V Missing data are explained, Non-significant data are reported | V No other source of bias | Moderate risk |
| Temel *et al.*, 2017 | V Centralized randomization | V | X Nonblinded RCT | X14% loss to follow up on ACP.  | V Missing data are explained, non-significant data are reported. | X Intervention patients were slightly older and had greater comorbidities | Moderate risk |
| Engelhardt *et al.*, 2006 | V Computerized | V  | X Nonblinded RCT | X 34% loss to follow up of ACP.  | V Non- significant data are reported | V Intention to treat analysis | Moderate risk |
| Radwany *et al.*, 2014 | NANot fully described | NANot fully described | X Nonblinded RCT | V Except deaths, there was no mention of loss to follow up | V Non- significant data are reported | X Small number of patients in each group. Baseline durable power of attorney rates higher in intervention group. Outcome measurement method not fully described.  | Very high risk  |

**X- Risk of bias**

**V- Low risk of bias**

ACP; Advance care planning

PC; Palliative care

ICU; Intensive care unit

DNR; Don not resuscitate

AD; Advance directives

RCT; Randomized controlled trial