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End of Life Care and Do Not Resuscitate Orders: How Much Does Age Influence Decision Making? A Systematic Review and Meta-Analysis

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Abstract

With population aging, "do not resuscitate" (DNAR) decisions, pertaining to the appropriateness of attempting resuscitation following a cardiac arrest, are becoming commoner. It is unclear from the literature whether using age to make these decisions represents "ageism." We undertook a systematic review of the literature using CINAHL, Medline, and the Cochrane database to investigate the relationship between age and DNAR. All 10 studies fulfilling our inclusion criteria found that "do not attempt resuscitation" orders were more prevalent in older patients; eight demonstrated that this was independent of other mediating factors such as illness severity and likely outcome. In studies comparing age groups, the adjusted odds of having a DNAR order were greater in patients aged 75 to 84 and ≥85 years (adjusted odds ratio [AOR] 1.70, 95% confidence interval [CI] = [1.25, 2.33] and 2.96, 95% CI = [2.34, 3.74], respectively), compared with those <65 years. In studies treating age as a continuous variable, there was no significant increase in the use of DNAR with age (AOR 0.98, 95% CI = [0.84, 1.15]). In conclusion, age increases the use of "do not resuscitate" orders, but more research is needed to determine whether this represents "ageism."

Keywords

age discrimination/stereotypes, decision making, mortality, palliative care, quality of life

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Introduction

Although the factors affecting decisions around resuscitation have been extensively studied, the role of age remains controversial. Whether a patient undergoes cardiopulmonary resuscitation (CPR) depends on many factors, including patient preferences, predicted success rate, and the risks of the procedure versus the perceived benefit (Bruce-Jones, 1996). To help patients make an informed decision, physicians must incorporate these factors into their decision making. Older patients are less likely to be resuscitated following a cardiac arrest than younger people in similar circumstances (Hakim et al., 1996). This might be due to their higher mortality, but some authors argue that it constitutes "ageism" on the part of medical practitioners (Mackay, Powell, Charman, & Rozario, 2004). Defined as "A process of systematic stereotyping of and discrimination against people because they are old, . . ." ageism can manifest in health care through the withholding of treatment solely on the basis of age (Butler, 1975, p. 173). In resuscitation, decisions against active resuscitation based purely on a patient's chronological age without considering probability of survival, quality of life, or patient wishes may constitute ageism.

Since its adoption, the success rate of CPR has declined, partly due to the more widespread use of the technique (Lannon & O'Keeffe, 2010). CPR was developed primarily to restart the heart and breathing of patients who suffered an acute insult leading to cardiac arrest, but is now used in many patients who have had a slower and more predictable decline, in whom the chances of success are much lower (Watkins, 2001). Given CPR's low success rate and the high risk of

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complications, many authors argue that this technique should be used much more selectively (Bossaert et al., 2015; Watkins, 2001). However, deciding on the appropriate patients to resuscitate depends on myriad factors, including prognosis, general health, functional status, and the wishes of patients and their relatives (De Decker, Annweiler, Launay, Fantino, & Beauchet, 2014).

Do not attempt resuscitation (DNAR) orders allow patients and doctors to make rational decisions about the appropriateness of CPR, which may be ethically unjustifiable in situations where it is unacceptably futile and inappropriately aggressive (Bossaert et al., 2015; Htut, Shahrul, & Poi, 2007; Mattes, Tung, Baum, Parikh, & Ashamalla, 2014). Professional organizations support the appropriate use of DNAR orders. The General Medical Council (GMC) of the United Kingdom has issued guidance on their use ("Treatment and Care," 2010).

The use of DNAR orders varies widely. Only 6.2% of cancer patients referred for palliative radiotherapy in Toronto had an active DNAR order in place (Bradley et al., 2006). In contrast, 15% of patients at a Level-1 trauma center in Denver had DNAR orders (7% were preexisting and 8% initiated during the current admission; Salottolo et al., 2015). The incidence of DNAR orders in intensive care unit (ICU) setting has varied from 9.3% to 11.7% (Boyd, Teres, Rapoport, & Lemeshow, 1996; Quill, Ratcliffe, Harhay, & Halpern, 2014). The reasons for variation in prevalence are not fully understood, but probability of survival, quality of life, and age are often quoted (Rozzini et al., 2005).

Medical practitioners are more frequently called upon to make decisions about resuscitation of older people as life expectancy increases. A quarter of the world's population will be aged 60 years and older by 2050, including 1:3 people in developed countries ("World Population Aging 2013," 2013). However, there is no independent association between mortality after CPR and age (Murphy, Murray, Robinson, & Campion, 1989). Rather, age is strongly associated with increased comorbidity, functional decline, and frailty, all of which decrease the likelihood of survival after CPR (Hakim et al., 1996). In these circumstances, deciding not to resuscitate patients solely based on their age would seem inappropriate.

There is no consensus in the literature regarding medical practitioners' approach to age and resuscitation. Some authors observe that age affects decisions about resuscitation and suggest that this constitutes ageism, whereas others reject this assertion (Gunderson, Tomkowiak, Menachemi, & Brooks, 2005; Mackay et al., 2004; Thompson & Jenner, 1994). Given this uncertainty, we conducted a systematic review of the literature to determine if age is independently correlated with the use of DNAR orders in critically ill patients.

Method

This study is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement for systematic reviews (Moher, Liberati, Tetzlaff, & Altman, 2009). The aim was to determine whether older critically ill patients were more likely to have DNAR orders than comparable younger patients.

Population, Intervention, Comparator, Outcome (PICO) Question

The PICO question was as follows:

> *In seriously ill or hospitalized patients, in whom end of life care is relevant* (population), *are older patients* (intervention/exposure) *more likely to have do-not-attempt resuscitation orders* (outcome) *than younger patients* (comparator)?

Search Strategy

A systematic review of the literature was conducted through Medline (via OvidSP), the Cochrane Library, and CINAHL (via EBSCO). The electronic search was supplemented by a manual search of reference lists of relevant articles. All relevant articles between January 1990 and September 2016 were included. Although "DNAR" orders were used prior to 1990, they were far less common, and much current thinking has been developed since the latter half of the 1990s. It thus seemed inappropriate to include articles prior to this date. Appendix A shows the search terms used for each element of the PICO question. Appendix B shows the search strategies used in each database.

Observational studies that assessed the age of patients and whether or not a DNAR order was placed were included. The main aim of this review was to investigate clinicians' use of DNAR orders in "real life" situations. Interventional studies were not included as they would have focused on the implementation of new or different ways of working and not reflected normal clinical practice. Inclusion criteria were as follows: if the studies analyzed factors other than age, that could affect a clinician's decision-making process; if a comparison was made between a DNAR and non-DNAR group on the basis of age or if the study compared different age groups of patients. Only studies reported in English or translated to English were included in the review.

Hypothetical studies of physician decision making, studies only investigating the patient perspective of decision making, and those that did not include patients <65 years were excluded from this review. Studies using age cutoffs of 65 years were included in the meta-analysis, while studies using different age cutoffs were only included in the narrative synthesis.

Data Extraction, Reporting of Outcome, and Critical Appraisal

Data were extracted by the five primary researchers (I.C., A.K., L.L., M.M., and G.M.), and checked by the research supervisor (I.S.), using a standardized form (Appendix C). Disagreements were resolved through consensus. Studies were critically appraised using the Critical Appraisal Skills Program (CASP) checklist for assessing cohort studies (A. Hill et al., n.d.). The proportion of patients in each age group who had a DNAR order and the adjusted likelihood of having a DNAR order were recorded when reported in the study.

Meta-Analysis of Data

Data from studies presenting age in comparable formats were meta-analyzed to determine the overall association between age and the likelihood of having a DNAR order. Results were presented as forest plots. Statistical heterogeneity was assessed using the I^2 and Cochran Q statistics. A funnel plot of studies and subgroups included in the meta-analysis was produced to detect publication bias.

Results

Of the 612 unique studies identified, 10 were included in the final review (Appendix D: PRISMA flow diagram).

Overview of Studies Included in the Review

Eight studies were retrospective observational studies that investigated patient's medical charts or records, while two were prospective (Brizzi et al., 2012; Hamel et al., 2000). Four were multicenter studies (Boyd et al., 1996; Dean, Martinez, & Newgard, 2015; Hakim et al., 1996; Quill et al., 2014). Sample size ranged from 109 to 269,002 patients. Most studies investigated hospital inpatients, including three studies analyzing patients from ICUs (Boyd et al., 1996; Koch, Rodeffer, & Wears, 1994; Quill et al., 2014). Five studies investigated patients with specific medical conditions, including intracerebral hemorrhage (ICH; two studies), severe traumatic brain injury (TBI), stroke, and kidney failure (Alexandrov, Bladin, Meslin, & Norris, 1995; Anderson, Sikorski, & Finucane, 2006; Brizzi et al., 2012; Dean et al., 2015; Yang, Li, & Guo, 2015).

Nine studies used logistic regression to analyze factors associated with DNAR decisions. The final study (Koch et al.) used log-linear modeling to identify associations between variables, but did not quote the adjusted odds ratios from their model in their results (Koch et al., 1994). Table 1 summarizes the mediating factors included in the multivariate analyses of each study.

Summary of the Individual Study Findings

Koch et al. described the changes in terminal care in a single ICU in the United States between 1984 and 1988 (Koch et al., 1994). All 2,185 patients were under the care of the same two physicians, reducing variations in individual physician's attitudes as a potential source of bias. The study examined factors that might influence the implementation of DNAR orders including age, race, sex, diagnosis, and acuity of illness (measured by the organ failure index). Although increasing age was correlated with DNAR orders (5.72% of <65-year-olds vs. 19.46% of those ≥65 years), this was not independent of other mediating factors. The authors suggest that the increased incidence of diseases like cancer and cardiovascular disease accounted for the increase in DNAR orders in older people. The most common reason for DNAR orders were multiple organ failure and neurological dysfunction.

Alexandrov et al. studied 450 consecutive stroke patients admitted to a single hospital in Canada. They found a significant difference in the prevalence of DNAR orders between patients aged ≥60 years with those <60 years, independent of the clinical severity of the patients' condition. The authors did not quote the odds ratios for DNAR orders in their results (Alexandrov et al., 1995).

Boyd et al. investigated the association between age and DNAR orders in ICU patients in the United States and Europe, using two separate databases: the mortality prediction model (MPM) database (6,103 patients) and the European–North American Study of Severity Systems (ENAS) database (3,226 patients; Boyd et al., 1996). MPM recorded DNAR orders at discharge, whereas the ENAS database recorded DNAR orders 24 hr after admission. For both databases, there was an increase in the unadjusted probability of having a DNAR order with increasing age (Table 2). However, after adjusting for illness severity and predicted prognosis using the MPM survival probability (mortality prediction model survival probability [MPMo]) there was no significant difference in the odds of having a DNAR order for patients aged 65 to 74 years compared with those aged 18 to 65 years. The adjusted odds of having a DNAR order was, however, significantly greater for those aged ≥85 years (adjusted odds ratio = 2.8) in the ENAS database, and in the 75 to 84 years and ≥85 years age groups in the MPM database (adjusted odds ratios 1.5 and 2.4, respectively).

Hakim et al. studied 6,802 seriously ill patients across five different hospitals, and found that DNAR orders in patients ≥85 years were twice as common as in those aged <75 years, independent of disease category, functional impairment, quality of life, patient preference, or prognosis. The main aim of this study was to determine time to initial DNAR decision. This was the only study that looked at patient preferences as a mediating factor (Hakim et al., 1996).

Table 1. Summary of the Mediating Factors Included in the Multivariate Analysis for Each Study.

		Mediating factors included in the multivariate analysis													
Study	Sample size	Age	Race	Gender	Presenting complaint/reason for admission	Medical versus surgical condition	Illness severity	Comorbidities	Reason for DNAR decision	Probability of survival	Socioeconomic status	Functional capacity	Quality of life	Patient preference	Hospital status
Alexandrov	450	√					√								
Anderson	109	√	√	√	√			√				√			
Boyd	9,527	√				√	√			√					
Brizzi	197	√		√			√	√							
Dean	71,275	√													√
Hakim	6,802	√			√		√			√	√			√	
Koch	2,185	√	√	√	√				√						
Quill	269,002	√	√	√		√	√			√	√	√			
Vetsch	882	√		√				√				√			
Yang	759	√		√			√	√							

Note. DNAR = do not attempt resuscitation.

Table 2. Summary of Studies Included in the Systematic Review.

Article	Year of publication	Database	Type of study	Main aim of study	Patient group and sample size	Comparator	Main outcome measure	Main findings
"Changing Patterns of Terminal Care Management in an Intensive Care Unit." Koch, Rodeffer, and Wears	1994	Medline	Retrospective single center observational study	To describe changes in terminal care management over time	2,185 patients that were admitted to an ICU unit over a time period of 4 years (March 1984-June 1988)	Patient characteristic variables included age, race/ethnicity (Black/Caucasian), sex (m/f), reason for ICU admission	Percentage of patients in each age group that had a DNAR order in place. This was also assessed after adjustment for admission diagnosis and reason for DNAR	Percentage of patients on DNAR orders increased with age (14-55 years: 4.55%; 56-65 years: 12.25%; 66-75 years: 16.77%; >75 years: 25.74%—$p < .0001$). No significant difference between age groups was seen when adjusted for admission diagnosis and reason for DNAR order.
"Do-Not-Resuscitate Orders in Acute Stroke." Alexandrov, Bladin, Meslin, and Norris	1995	CINAHL	Observational study (not clear if retrospective or prospective)	To evaluate the clinical factors associated with DNAR orders in acute stroke patients during their hospital stay	450 consecutive patients admitted to a single hospital in Canada	Patients aged >60 years and those aged ≤60 years	Proportion of DNAR orders in each group; adjusted odds of having a DNAR order	No patients <60 years had DNAR orders; the adjusted odds of having a DNAR order was greater in patients aged >60 years, but the actual odds ratio was not stated.
"The Relationship Between Age and the Use of DNR Orders in Critical Care Patients. Evidence for Age Discrimination." Boyd, Teres, Rapoport, and Lemeshow	1996	CINAHL	Retrospective, multicenter observational study	To determine whether a relationship exists between the use of DNR orders in the ICU and the age of the patient after controlling for the severity of illness	This was a parallel analysis of two independent databases: The MPM database (6,103 patients in four large hospitals in the United States), and the ENAS database (3,226 patients in 25 U.S. hospitals)	Age: <65 years, 65 to 74, 75 to 84, >85 Illness severity using the MPMo	Logistic regression modeling with DNAR status as the dependent variable	Percentage of patients on the MPM database on DNAR orders increased with age: 18 to <65 years: 8.0%; 65 to <75 years: 11.2%; 75 to <85 years: 18.9%; ≥85 years: 32.6%. Percentage of patients on the ENAS database on DNAR orders increased with age: 18 to <65 years: 4.2%; 65 to <75 years: 4.2%; 75 to <85 years: 8.8%; ≥85 years: 15.4%. On multivariate analysis, there was no significant difference in the adjusted probability of having a DNAR order at ICU discharge between patients aged 18 to <65 years and those aged 65 to >75 years. Using the MPM database, the adjusted odds of having a DNAR order for patients 75 to < 85 years (1.5) ≥85 years (2.4) was significantly higher than for patients 18 to <65 years. For the ENAS database, the adjusted odds for having a DNAR order was significantly higher for patients aged ≥85 years (2.8).
"Factors Associated With Do-Not-Resuscitate Orders: Patients' Preferences, Prognoses, and Physicians' Judgments." Hakim et al.	1996	Manual search	Prospective observational study	To examine the association between patients' preferences for resuscitation (along with other patient and physician characteristics) and the frequency and timing of DNR orders	6,802 patients with serious illness attending one of five tertiary hospitals in the United States	10-year age groups compared: <55 years; 55 to 64 years, 65 to 74 years and ≥85 years	Adjusted odds of patients having a DNAR order; adjusted time ratio of patients having a DNAR order	Patients aged ≥85 years were twice as likely to have a DNAR order than those aged <75 years. Using age <55 years as a reference, time to DNAR order was significantly shorter for all higher age groups.
"DNR Orders at a Tertiary Care Hospital—Are They Appropriate?" Vetsch, Uehlinger, and Zenklusen.	2002	Medline	Retrospective clinical chart review	To investigate the epidemiology, manner of application, and appropriateness of DNAR orders	882 patients admitted under internal medicine during four randomly selected months in 1998 (Group 1) and all patients under internal medicine who died during 1998 (172 patients—Group 2)	No comparator—age was presented as a continuous variable	Adjusted odds of having a DNAR order with increasing age	For patients in Group 1, the adjusted odds of having a DNAR order increased by 1.08 (95% CI = [1.06, 1.11]) with each additional year, while for Group 2, the odds increased by 1.06 (95% CI = [1.03, 1.09])

(continued)

Table 2. (continued)

Article	Year of publication	Database	Type of study	Main aim of study	Patient group and sample size	Comparator	Main outcome measure	Main findings
"Advance Care Planning by or on Behalf of Peritoneal Dialysis Patients in Long-Term Care." Anderson, Sikorski, and Finucane	2006	Manual search	Retrospective, single center observational study	To examine factors influencing ACP and the effect of those plans on patient outcomes	109 peritoneal dialysis patients admitted to an academic nursing home between 1986 and 2000	Patient characteristic variables included age, sex, race, presence of comorbid conditions, and ADL score	Patients allocated to four groups (Group A = no limits on treatment, Group B = DNAR order, Group C = DNH and DNAR orders are written, and Group D = patients receive only measures that aim to provide comfort and preserve dignity	In univariate analyses, having a DNAR status was associated significantly with increased age (68.5 ± 12.2 vs. 59.5 ± 12.1 years; $p < .003$). In the multivariate logistic model, older age (odds ratio, 1.04; CI = [1.0007, 1.09]), lower functional ADL score (odds ratio, 1.22; CI = [1.08, 1.38]), and coronary artery disease (odds ratio, 4.24; CI = [1.49, 12.02]) were significant independent predictors of having a DNAR order.
"Early Do-Not-Resuscitate Orders in Intracerebral Haemorrhage; Frequency and Predictive Value for Death and Functional Outcome. A Retrospective Cohort Study." Brizzi et al.	2012	Manual search	Prospective observational study	To determine the frequency and predictive factors of DNR orders and its association to prognosis	197 consecutive ICH patients admitted to Skåne University Hospital, Malmö, Sweden, between January 2007 and June 2009	Age cohorts compared: <75 years and ≥75 years	Adjusted odds of having a DNAR order	Adjusted odds of having a DNAR order for patients aged ≥75 years were 4.2 (95% CI = [1.8, 9.6]) compared with those <75 years
"Variation in Decisions to Forgo Life-Sustaining Therapies in U.S. ICUs." Quill, Ratcliffe, Harhay, and Halpern	2014	Medline	Retrospective, multicenter observational study	To create a multivariable model for DFLST and then calculate adjusted rates of DFLST for each ICU in the study	269,002 patients admitted to 153 ICUs in the United States between 2001 and 2009	Patient characteristic variables included age race/ethnicity, sex, functional status on ICU admission insurance, source of ICU admission, and patient type	The primary outcome was a DFLST, defined as any change in "code status" from no limitations on care at the time of ICU admission to any limitation(s) on care prior to ICU discharge	Using a reference age of <65 years, the adjusted odds for having a DFLST for older age groups were 65 to 74 years: 1.50 (95% CI = [1.43, 1.58]); 75 to 84 years: 2.18 (95% CI = [2.07, 2.30]); ≥85 years: 3.44 (95% CI = [3.23, 3.67]).
"Do Not Resuscitate Orders for Patients With Intracerebral Hemorrhage: Experience From a Chinese Tertiary Care Center." Yang, Li, and Guo.	2015	Medline	Retrospective single center observational study	To determine the factors influencing the implementation of DNAR orders in patients with ICH at a university hospital in China	759 patients admitted with ICH from June 2010 to December 2012	Patient characteristic variables included age, sex, GCS on arrival, ICH volume, and location of ICH	Binary logistic regression analysis was conducted to identify factors associated independently with the decision to establish a DNR order	Patients with DNAR orders were older on average compared with those with no DNR order. (73.1 ± 10.1 vs. 56.0 ± 13.2 years). On multivariate logistic regression, the adjusted odds of having a DNAR order was 0.84 (95% CI = [0.81, 0.88]; $p < .001$).
"Variability in Early Do Not Attempt Resuscitation Orders Among Patients With Serious Traumatic Brain Injury." Dean, Martinez, and Newgard	2015		Retrospective observational study		71,275 patients with serious TBI admitted to 141 hospitals in the United States	Patients compared by age group (<1 year, 1-17 years, 18-34 years, 35-64 years, ≥65 years)	Logistic regression estimates of having a DNAR order	Estimates, using age ≥65 years as reference: 35 to 64 years: –1.89 (95% CI = [–2.08, –1.70); 18 to 34 years: –2.60 (95% CI = [–2.85, –2.35]; 1 to 17 years; –2.94 (95% CI = [–3.33, –2.55]); <1 year: –3.68 (95% CI = [–5.64, –1.72]).

Note. DNAR = do not attempt resuscitation; ICU = intensive care unit; DNR = do not resuscitate; MPM = mortality prediction model; ENAS = European–North American Study of Severity Systems; ACP = advance care planning; ADL = activities of daily living; DNH = do not hospitalize; CI = confidence interval; ICH = intracerebral hemorrhage; MPMo = mortality prediction model survival probability; DFLST = decision to forgo life-sustaining therapy; GCS = Glasgow Coma Scale; TBI = traumatic brain injury.

Vetsch et al. investigated the association between DNAR orders and age, clinical presentations, and comorbidities in 882 patients admitted to an internal medicine unit in Sweden. The authors found a significant association with age and DNAR orders, which was independent of gender, comorbidities, and functional capacity. The adjusted odds of having a DNAR order increased by 1.08 (95% confidence interval [CI] = [1.06, 1.11]) with each additional year of life (Vetsch, Uehlinger, & Zenklusen, 2002).

Anderson et al. retrospectively investigated factors influencing advanced care planning in 109 dialysis patients admitted to a single nursing home (Anderson et al., 2006). Age was treated as a continuous variable. The mean age of patients with a DNAR order was 68.5 ± 12.2 years versus 59.5 ± 12.1 years for those without ($p < .003$). After adjusting for race, gender, presenting complaint, and comorbidities, the odds ratio of having a DNAR order was 1.04 (95% CI = [1.01, 1.09]) per additional year of life.

Brizzi et al. (2012) assessed 197 consecutive patients with ICH admitted to Skåne University Hospital, Malmö, Sweden, between January 2007 and June 2009. Patients aged ≥75 years were significantly more likely to have a DNAR order (adjusted odds ratio 4.2 (95% CI = [1.8, 9.6]), independent of illness severity and comorbidities.

Quill et al. (2014) studied variations in end-of-life decision making across ICUs in the United States. Data from 269,002 patients admitted to 153 ICUs between 2001 and 2009 were retrospectively analyzed. The authors used multivariate logistic regression to identify variables affecting the decision to forgo life-sustaining therapies (DFLSTs). DFLST always included, but were not limited to do not resuscitate (DNR) orders, as decisions to restrict therapy and decisions to implement only comfort therapy were also included. Age was significantly associated with having a DFLST, independent of race, gender, clinical presentation, social status, illness severity, functional status, and prognosis. Using a reference age of <65 years, the adjusted odds for having a DFLST for older age groups were 65 to 74 years: 1.50 (95% CI = [1.43, 1.58]), 75 to 84 years: 2.18 (95% CI = [2.07, 2.30]), ≥85 years: 3.44 (95% CI = [3.23, 3.67]). The large sample size and multicenter design makes the results of this study more likely to be generalizable. Data were collected through project IMPACT, a voluntary, fee-based data collection system used across the United States to collect standardized data on ICU patients. Illness severity was clearly defined, using the MPM-III. Thus, data collection and interpretation were comparable across all hospital sites included in this study. In addition, this is a relatively recent study so attitudes toward end-of-life care in the study are likely to be similar to current attitudes.

Yang et al. (2015) investigated DNAR status in 759 patients with ICH. Patients with DNAR orders were older (73.1 ± 10.1 vs. 56.0 ± 13.2 years). However, after adjusting for gender, illness severity, and comorbidities, the odds of having a DNAR order decreased with increasing age (odds ratio of 0.84, 95% CI = [0.81, 0.88]).

Dean et al. investigated the use of DNAR orders in 71,275 patients with severe TBIs. Using age ≥65 years as a reference, the authors demonstrated that all younger age groups were significantly less likely have a DNAR order, independent of the level of hospital to which the patient was admitted (Table 2). However, the multivariate analysis did not include any patient mediating factors such as injury severity or premorbid status (Dean et al., 2015).

Meta-Analysis of Data

Two studies (Boyd et al., 1996, and Quill et al., 2014) used comparable age categories when analyzing their data. Combining the results of these studies, and using patients aged <65 years as a reference, patients aged 75 to 84 and those aged ≥85 years were more likely to have DNAR orders in place, independent of other mediating factors. However, there was no significant difference in the adjusted odds of having a DNAR order for patients aged 65 to 74 years (Figure 1 and Appendix E). The MPM and ENAS data from Boyd's study were included in the meta-analysis separately as these two data sets represent two independent studies.

Three studies (Vetsch et al. 2002, Anderson et al., 2006, and Yang et al., 2015) presented age as a continuous variable. The cumulative adjusted odds for having a DNAR order with increasing age was 0.98 (95% CI = [0.84, 1.15]), demonstrating no significant increase in the likelihood of DNAR with age. There was a high degree of statistical heterogeneity between studies included in this meta-analysis (Figure 2). In addition, the inclusion criteria were different: Vetsch studied all patients admitted to hospital under internal medicine, whereas Anderson's study only included patients on long-term dialysis, and Yang investigated a cohort with ICH.

Discussion

This review confirmed that age is an important determinant for the initiation of DNAR orders in critically ill patients, but whether this constitutes "ageism" remains unclear. The appropriateness of DNAR orders must be judged in conjunction with patient and carer preferences, quality of life issues, and probability of survival of individual patients, which were not consistently considered in the studies reviewed.

To fully understand the findings of these studies, we need to consider what factors, other than age, were considered in their analyses. Most studies included some measure of illness severity. For example, the two studies on ICH included either severity scoring systems for the ICH or a measure of conscious level (Brizzi et al., 2012;

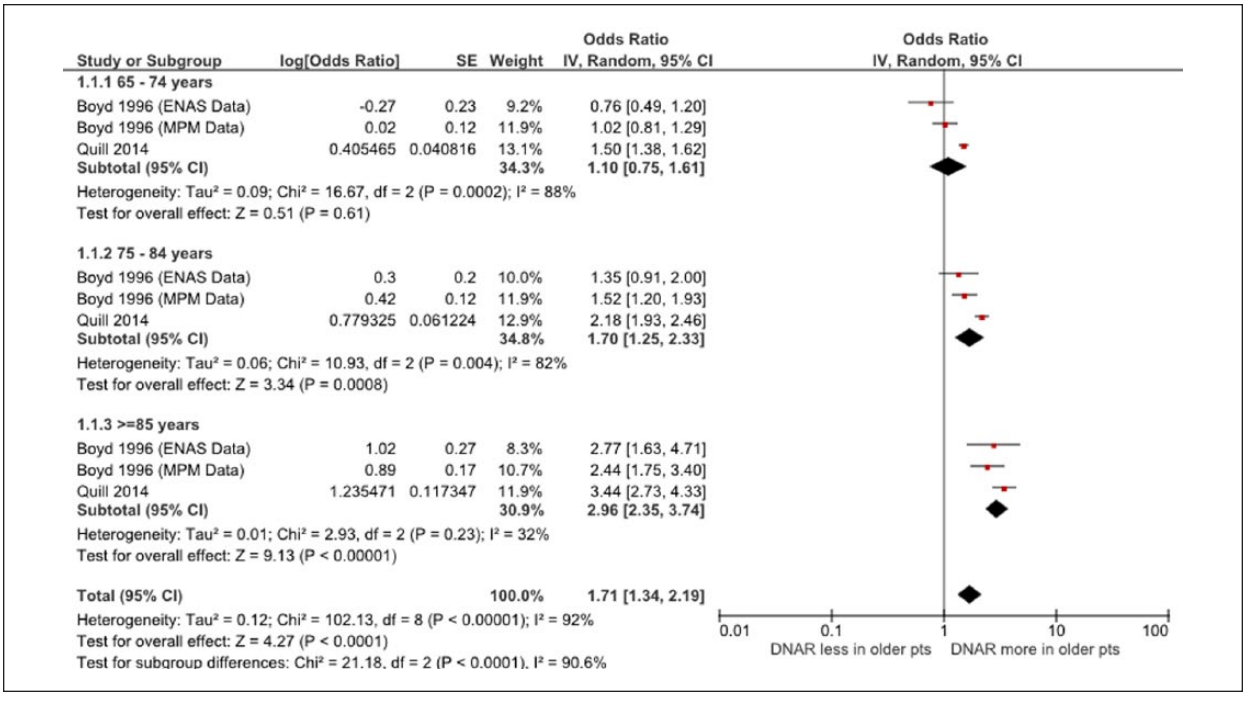


Figure 1. Forest plot of likelihood of DNAR with age for studies reporting age as a categorical variable.
Note. DNAR = do not attempt resuscitation; ENAS = European–North American Study of Severity Systems; MPM = mortality prediction model.

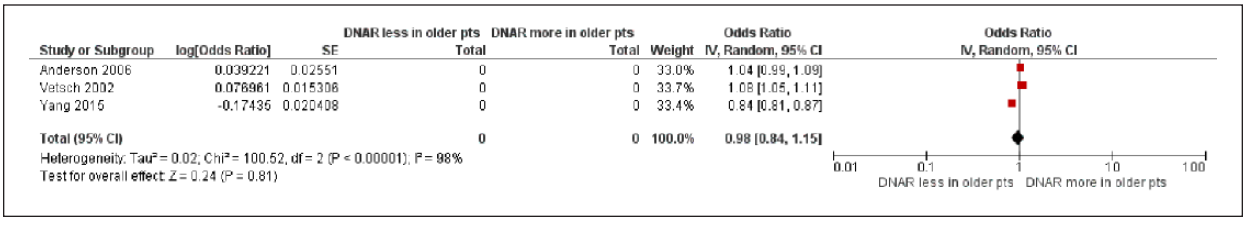


Figure 2. Forest plot of likelihood of DNAR with age for studies reporting age as a continuous variable.
Note. DNAR = do not attempt resuscitation.

Yang et al., 2015). Studies of inpatients and ICU patients also included measures of illness severity, such as the MPM-III score and organ failure scores, in their respective multivariate prediction models (Boyd et al., 1996; Koch et al., 1994; Quill et al., 2014). Other studies did not explicitly consider illness severity: While Vetsch et al. (2002) included patients' comorbidities in their analysis, they did not attempt to record illness acuity or severity. Dean's study of patients with severe TBI was primarily concerned with the variations in practice between different hospitals, and the authors admit that the omission of any measure of injury severity from their analysis would have limited the conclusions that could be drawn (Dean et al., 2015).

Other important factors that might have affected DNAR decisions, such as patients' premorbid status, quality of life, functional status, and probability of survival were not uniformly included in all studies (Table 1). Only three of the eight studies explicitly considered comorbidities in their analyses (Brizzi et al., 2012; Vetsch et al., 2002; Yang et al., 2015). However, two of the ICU studies used illness severity scores that included a measure of comorbidity (Boyd et al., 1996; Quill et al., 2014). Only four studies assessed patients' functional status (Anderson et al., 2006; Hakim et al., 1996; Quill et al., 2014; Vetsch et al., 2002). Apart from two of the ICU-based studies, which used the MPM-III as an estimate of illness severity, only one other study (Hakim et al.) included probability of survival in their analysis (Boyd et al., 1996; Hakim et al., 1996; Quill et al., 2014). In the absence of a uniform approach to risk adjustment, it is difficult to assess the appropriateness of decisions made, particularly as older patients are more likely to suffer from multiple comorbidities, loss of functional independence, and a decline in quality of life. Many authors have commented on the importance of these risk factors in

determining the appropriateness of resuscitation in older people (Hakim et al., 1996; Hamel et al., 2000; Rozzini et al., 2005). The lack of a positive association between age and DNAR in two of the studies is most likely explained by a failure to include all significant mediating factors in their analyses (Koch et al., 1994; Yang et al., 2015).

This review investigated real-life decision making by physicians. However, there is a parallel body of research investigating decision making using hypothetical scenarios. Most hypothetical studies also found a positive association between age and DNAR orders, not explained by mediating factors. A. Hill et al. (n.d.), surveying hospital doctors, found that "7 of the 24 senior staff would not resuscitate healthy patients aged over 70" (M. E. Hill, MacQuillan, Forsyth, & Heath, 1994, p. 1677). In a separate study, physicians were significantly more likely to choose DNAR for a 90-year-old compared with a 60-year-old patient who was equivalent to the older patient in all respects except age (67.7% vs. 7.4%; Moore, Wiggins, & Adams, 2015). We chose to concentrate on real-life decisions made by physicians rather than hypothetical scenarios as we were more interested in what physicians actually did, rather than what they thought they might do in a hypothetical situation.

Twelve studies comparing older and younger patients were excluded from the review (Appendix F). In two of these, the sample only included patients ≥65 years, and this did not allow comparisons of older and younger than 65 years. Both showed that DNAR orders were more common in older people, and that those ≥80 years were most likely to have DNAR orders in place, independent of their clinical status (Messinger-Rapport & Kamel, 2005; Oshitani, Nagai, & Matsui, 2014). Other studies demonstrated a univariate association between DNAR and age but did not adjust for mediating factors (Bacchetta, Eachempati, Fins, Hydo, & Barie, 2006; Reynolds, Hanson, Henderson, & Steinhauser, 2008; Siracuse et al., 2015; Solloway, Lafrance, Bakitas, & Gerken, 2005). Two studies looked at advanced directives other than DNAR orders; both found an increase in their use with age (Dunlay, Swetz, Mueller, & Roger, 2012; Hamel et al., 2000).

Only one of the studies included in this review considered the impact patients' preferences for CPR had on physicians' decisions (Hakim et al., 1996). Some researchers suggest that doctors often do not consult with patients about these decisions (Cherniack, 2002; Neuberger, Guthrie, & Aaronovitch, 2013). Whereas the GMC recommends that patients and their families should be involved in decision making, they are often excluded or coerced (Neuberger et al., 2013; "Treatment and Care," 2010). In this setting, patient autonomy may be neglected and decisions may be unduly influenced by physician bias. Conversely, the inappropriate imposition of CPR on patients who would rather avoid a potentially distressing and futile intervention at the end of life would also be considered a poor outcome. Reassuringly, Hakim's study suggests that patient preference was the most significant factor affecting time to DNAR decision in their cohort of seriously ill patients (Hakim et al., 1996).

Some qualitative studies excluded from this review also yielded results that shed light on clinician decision making. In focus groups of doctors and medical students, participants' views were influenced by age, medical condition, and likely outcome. Of concern, medical students were reluctant to involve patients and relatives in decisions, to protect them from unnecessary emotional stress (Tyrer, Williams, Feathers, Faull, & Baker, 2009). In another study, patient preferences were influenced by concerns about their primary diagnosis, quality of life, prognosis, and advancing age (Ebell, Smith, Seifert, & Polsinelli, 1990).

Age and ageism may play a part in decision making in other clinical settings. Physicians are less likely to provide aggressive emergency care for older patients with serious injuries (Giannoudis, Harwood, Court-Brown, & Pape, 2009; Kirkman et al., 2013). Negative attitudes have also been seen in general practice and acute hospital wards (Gott, Hinchliff, & Galena, 2004; Higgins, Der Riet, Slater, & Peek, 2007).

Limitations

There was significant methodological heterogeneity between studies in this review, particularly in relation to patients and settings. This was appropriate in many instances, as researchers sought to identify patient groups in whom DNAR orders were particularly relevant. In this regard, studies investigating patients with ICH, stroke, renal failure, and serious illness, as well as ICU-based studies were particularly useful (Anderson et al., 2006; Boyd et al., 1996; Brizzi et al., 2012; Hakim et al., 1996; Quill et al., 2014). However, this variation in sample populations may limit the generalizability of the findings to other contexts. Although the strict limitations on age criteria may have excluded some important studies, a review of these excluded studies (Appendix F) suggests that they supported the main findings of our review.

We only included articles either written in English or translated to English. However, the articles identified included papers from North America, Europe, and China, suggesting that the research identified were from both English speaking and non-English speaking countries. In addition, our resources did not permit a thorough search of the "gray" and unpublished literature on this topic.

Conclusion

The findings of this review should be interpreted with caution. On one hand, it raises the possibility that there is an unjustified bias against older people. On the other,

many of these decisions may be appropriate, when other factors are taken into account. Our review points to a need for further research to untangle these two contrasting interpretations. In particular, we need to compare decisions made by clinicians with the preferences of patients and carers. Researchers should also focus on other mediating factors that might affect this decision, including quality of life, probability of survival, comorbidities, and functional capacity. In this regard, a systematic approach to auditing DNAR orders (as described by Quill et al., but including a wider minimum data set) would help. Such an approach would also allow comparisons between hospitals and across national borders (Quill et al., 2014).

Appendix A

Elements of the PICO Question and Related Search Terms.

Heading	Variable from question	Search terms
Patient/ population:	Seriously ill or hospitalized patients in which end of life care is relevant	DNAR or DNACPR or DNR or do not attempt resuscitation or resuscitation orders or advance directive or resuscitation or cardiopulmonary resuscitation or do not resuscitate or do not attempt cardiopulmonary resuscitation
Intervention/ exposure:	Patients aged older than 65 years	Aged over 65 or age or aged or elderly or senior or older people or terminal care or end of life care
Comparator:	Patients aged younger than 65 years	
Outcome:	DNAR orders being set	Resuscitation decision or resuscitation decision making or factors
Setting:	Any	

Note. PICO = population, intervention, comparator, outcome; DNAR = do not attempt resuscitation; DNACPR = do not attempt cardiopulmonary resuscitation; DNR = do not resuscitate.

Appendix B

Search Strategies for CINAHL, Medline, and the Cochrane Library.

Database	Search strategy
CINAHL	(DNAR *OR* DNACPR *OR* DNR *OR* do not attempt resuscitation *OR* resuscitation orders *OR* advance directive *OR* resuscitation *OR* cardiopulmonary resuscitation *OR* do not resuscitate *OR* do not attempt cardiopulmonary resuscitation) *AND* (age *OR* aged *OR* elderly or senior *OR* older people *OR* terminal care *OR* end of life care) *AND* (resuscitation decision or resuscitation decision making)
Medline	(resuscitation orders *OR* DNAR *OR* cardiopulmonary resuscitation *OR* DNR *OR* DNACPR *OR* advanced directives) and (aged *OR* elderly *OR* age *OR* older *ADJ* people) *AND* ((decision *ADJ* making) *OR* (clinical *ADJ* decision *ADJ* making) *OR* decision) *AND* factors
The Cochrane Library	(Age *OR* elderly *OR* senior *OR* advanced age *OR* older or age over 65) *AND* ((DNAR *OR* DNACPR *OR* DNR *OR* do not attempt to resuscitate) *OR* (CPR *OR* cardiopulmonary resuscitation) *OR* (resuscitation order *OR* advanced directive)) *AND* (resuscitation decision *OR* resuscitation decision making)

Note. DNAR = do not attempt resuscitation; DNACPR = do not attempt cardiopulmonary resuscitation; DNR = do not resuscitate; CPR = cardiopulmonary resuscitation; ADJ = adjacent.

Appendix C

Data Extraction Tool Used in the Systematic Review.

General information	Date of data extraction
Identification features of the study Author	

(continued)

Appendix C (continued)

General information	Date of data extraction

Article title
Source (e.g., journal, conference) year/volume/pages/country of origin
Institutional affiliation (first author) and/or contact address
Identification of the reviewer
Notes
Specific information
Study characteristics
Verification of study eligibility
Population characteristics and setting
1. Target population (describe)
2. Inclusion criteria
3. Exclusion criteria
4. Recruitment procedures used (participation rates if available)
5. Characteristics of participants at intervention commencement
- Age
- Ethnicity
- Class
- Sex
- Other information
- Geographical region

6. Number of participants
7. Were intervention and control groups comparable?

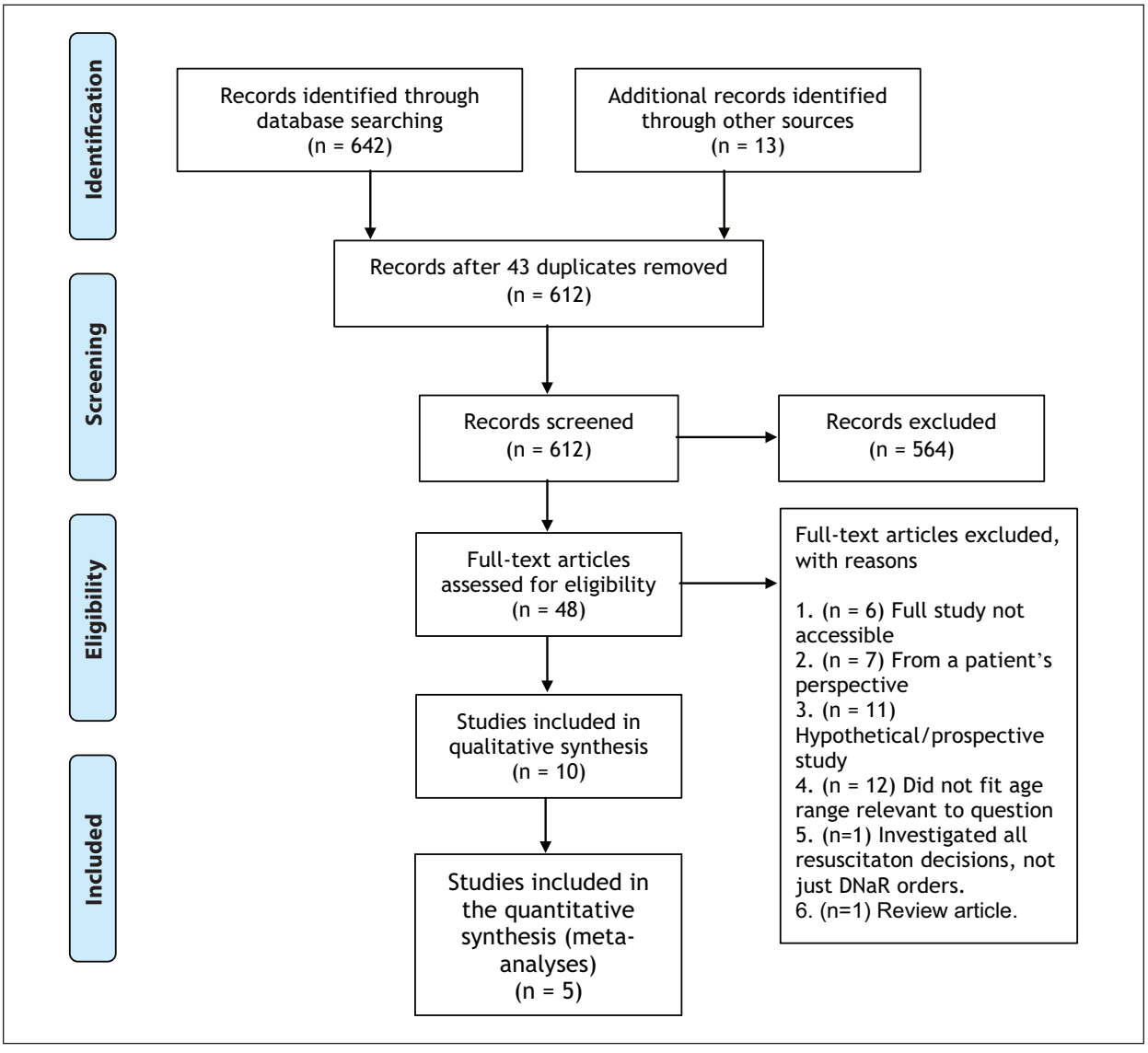
Methodological quality of the study
Interventions
1. Focus of intervention
2. Intervention site
3. Delivery mode of intervention
4. What mediating variables were investigated (if any)
5. Staff types

Outcomes, outcome measures
1. What was measured at baseline?
2. What was measured after the intervention?
3. Who carried out the measurement?
4. What was the measurement tool?
5. Was/were the tool(s) validated and how?

Analysis
1. Statistical techniques used
2. Does technique adjust for confounding?
3. Unit of analysis
4. Attrition rate (overall rates)
5. Was attrition adequately dealt with?
6. Number (or %) followed up from each condition

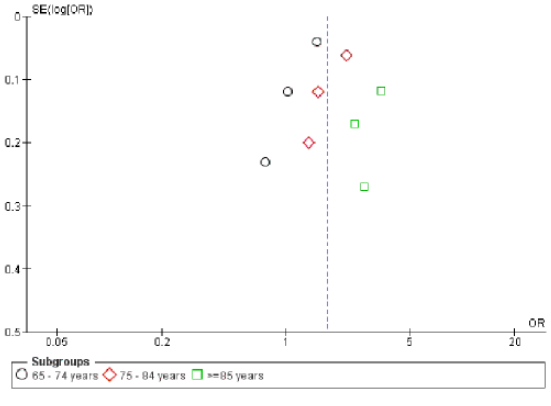
Results
Quantitative results (e.g., estimates of effect size)
Effect of the intervention on other mediating variables
Qualitative results
Cost of intervention
Cost-effectiveness
Notes

Appendix D



PRISMA flow diagram for the systematic review.
Note. PRISMA = preferred reporting items for systematic reviews and meta-analyses.

Appendix E



Funnel plot for studies included in the meta-analysis.

Appendix F

Summary of Studies Which Compared DNAR Likelihood With Age, but Were Excluded From the Analysis, With Reasons for Exclusion.

Paper	Year of publication	Database	Type of study	Main aim of study	Patient group and sample size	Comparator	Main outcome measure	Main findings	Reason for exclusion
"Do Not Resuscitate': How? why? and When?" Skerritt and Pitt	1997	Medline	Cross-sectional observational study	To look at who received DNR orders and how such decisions were taken and recorded in an inner-city district hospital	All inpatients (139; age range 16 ± 100 years) in an inner-city district general hospital on a single day	Age was presented in cohorts: <50 years and in 5-year cohorts from 51 to 100 years	Percentage of patients in each age group with a DNAR order	DNR patients were significantly older (81-84 years vs. 76.3 years, $p < .03$) and more likely to suffer from malignant and cardiorespiratory disease	The likelihood of having a DNAR order was not adjusted for concomitant disease or other risk factors
"Age-Related Differences in Care Preferences, Treatment Decisions and Clinical Outcomes of Seriously Ill Hospitalized Adults: Lessons From SUPPORT." Hamel et al.	2000	Medline	Observational prospective study	To determine patient and physician preferences in resuscitation decisions, including the rate of instituting DNAR orders	9,105 seriously ill hospitalized adults	For DNAR orders, patients aged ≥85 years were compared with those aged <75 years	Adjusted odds of having a DNAR order	The adjusted probability of having a DNR order written by study day 30 was twice as high for patients 85 years and older compared with patients younger than age 75 years	This study looked at age-related differences in the timing and likelihood of advanced directive, but not DNAR orders primarily
"Resuscitation After Cardiac Surgery: Are We Ageist?" Mackay, Powell, Charman, and Rozario	2004	Medline	Retrospective observational study	To investigate the influence of age and other factors of the Parsonett score in determining the incidence and outcome of cardiac arrest	6,550 patients undergoing open heart surgery in a tertiary cardiothoracic unit in England, over 4 years, commencing April 1996	Patients ≥70 years and those <70 years	Percentage of patients who died without CPR	Cardiopulmonary resuscitation was withheld in 46% of older adults (70 years or over) versus 40% of younger deaths, which represented 3.1% of older adults versus 2.1% of younger patients	The study did not look at the incidence of DNAR orders in all patients, only the withholding of CPR in patients who had died. Did not specifically compare patients ≥65 with those <65 years
"A Chart Review of Seven Hundred Eighty-Two Deaths in Hospitals, Nursing Homes, and Hospice/Home Care." Solloway, Lafrance, Bakitas, and Gerken	2005	Medline	Retrospective clinical chart review	To determine if the experience of dying differed among settings in New Hampshire, USA	742 deaths in hospitals, nursing homes, and home care/hospice agencies during February and March 2002	Use of DNAR orders, living wills, and DPAHC orders in different settings	Age of patients with DNAR orders.	Two thirds of patients with a DNAR order, living will, or DPAHC order were 75 years and older	The article did not directly compare age between those with and without DNAR orders; no adjustment was made for severity of illness. Age cutoff used was 75 years

(continued)

Appendix F (continued)

Paper	Year of publication	Database	Type of study	Main aim of study	Patient group and sample size	Comparator	Main outcome measure	Main findings	Reason for exclusion
"Predictors of Do Not Resuscitate Orders in the Nursing Home." Messinger-Rapport and Kamel	2005	Manual Search	Cross-sectional clinical chart review	To determine the prevalence of DNR orders, and predictors of DNR orders in older institutionalized individuals in a large community teaching nursing home	177 consecutively located older patients from an 899-bed academic long-term care facility	Age cohorts compared: Patients aged <85 years and those aged ≥85 years	Adjusted odds of having a DNAR order	DNAR orders were more prevalent in older patients (57% vs. 30%, $p < .05$). The adjusted odds of having a DNAR order was significantly higher in patients aged ≥85 years (B = −1.0; $p = .017$)	The study only included older patients (aged ≥65 years)
"Factors Influencing DNR Decision-Making in a Surgical ICU." Bacchetta et al.	2006	CINAHL	Prospective observational study	To determine the clinical factors that influenced the presence of a DNR order in the surgical ICU	195 patients with a DNAR order admitted to the surgical ICU of a teaching hospital, and 215 patients without a DNAR order who died during their admission. Data collected from May 1, 1991 to May 1998	Patients admitted to the surgical ICU with a DNAR order and those without a DNAR order who died during their admission	Mean age of patients with DNAR orders and those without	Mean age of DNAR patients was 69.9 years versus 67.5 years for non-DNAR patients	Study only included non-DNAR patients who died; the adjusted odds ratio of having a DNAR order could not be ascertained due to the way the sample was defined. Mean age of both groups was ≥65 years
"End-of-Life Care in Nursing Home Settings: Do Race or Age Matter?" Reynolds, Hanson, Henderson, and Steinhauser	2008	Manual search	Retrospective clinical chart review	To test whether racial and/or age-based differences in end-of-life care exist in nursing home settings	1,133 nursing home residents	Age cohorts compared: <79 years; 80-87 years; ≥88 years	Percentage of patients with DNAR orders	Percentage of patients with DNAR orders: <79 years = 44.7%; 80 to 87 years = 64.0%; ≥88 years = 77.1%	The likelihood of having a DNAR order was not adjusted for concomitant disease or other risk factors
"In Hospital Cardiac Arrest: Factors in the Decision Not to Resuscitate. The Impact of an Organised In-Hospital Emergency System." Mendes et al.	2009	Manual Search	Retrospective observational study	To identify factors associated with DNAR decisions in patients who suffer cardiac arrest	227 medical emergency team calls for cardiac arrest between January 2002 and August 2006	Patients in whom CPR not started were compared with those who received CPR	Mean age of each cohort	In patients who did not receive CPR, the mean age was 80 years, compared with 71 years in those receiving CPR	Likelihood of receiving CPR was not adjusted for other risk factors; This study compared the decision to commence CPR at the time of cardiac arrest, not the use of DNAR orders
"Survey of Do-Not-Resuscitate Orders in Surgical ICUs." Huang, Huang, and Ko	2010	Medline	Retrospective observational study	To survey each aspect of DNR, determine the clinical factors that influence DNR consent, and assess the impact of DNR consent on treatment in the surgical ICU	14,698 patients, aged ≥18 years, admitted to an ICU between January 2003 and December 2006	Patients without DNAR orders	Mean age of patients with and without DNAR orders	The mean age of patients with DNR was 62.5± 16.5, whereas patients without, was 58.6±17.0	The study did not adjust for other significant factors, such as illness severity, probability of survival, or patient preferences. The mean age of each group was < 65 years

(continued)

Appendix F (continued)

Paper	Year of publication	Database	Type of study	Main aim of study	Patient group and sample size	Comparator	Main outcome measure	Main findings	Reason for exclusion
"Advance Directives in Community Patients With Heart Failure." Dunlay, Swetz, Mueller, and Roger.	2012	CINAHL	Prospective, longitudinal observational study	To test the hypothesis that ADs specifying limits in the aggressiveness of care patients wished to receive at the end of life were associated with decreased end-of-life hospitalizations, ICU admissions, and mechanical ventilation	608 patients in Olmsted County, Minnesota, presenting with cardia failure	Age was compared in 10-year cohorts	Adjusted odds ratio of having an AD	There was an increase in the adjusted odds of having an AD of 1.82 for each increase in age of 10 years	ADs included decisions on ICU admission and mechanical ventilation and were not restricted to DNAR orders. There was no attempt to define the frequency of ADs in specific age groups
"Rationale for Physicians to Propose Do-Not-Resuscitate Orders in Elderly Community-Acquired Pneumonia Cases." Oshitani, Nagai, and Matsui.	2014	Medline	Retrospective observational study	To elucidate the factors influencing physicians' proposal for DNR orders and their validity as a prognostic predictor, by comparing older adult pneumonia cases with and without DNAR orders	641 community-acquired pneumonia patients aged 65 years or older	Compared patients aged ≥75 years with those aged 65 to 74 years	Adjusted odds of having a DNAR order	The adjusted odds of having a DNAR order was 1.99 (95% CI = [1.09, 3.63])	This study only included patients aged ≥65 years
"Impact of 'Do Not Resuscitate' Status on the Outcome of Major Vascular Surgical Procedures." Siracuse et al.	2015	Medline	Prospective observational study	To assess outcomes in DNR patients undergoing major vascular procedures	110,279 patients undergoing common major vascular procedures were identified in the 2007 to 2010 National Surgical Quality Improvement Project databases	Patients aged ≥80 years compared with those aged <80 years	Percentage of patients with DNAR orders	DNR patients were more likely to be functionally dependent (69% vs. 15%; $p <$ .0001), ≥80 years of age (53% vs. 20%; $p <$ .001), and suffer from a variety of cardiac, pulmonary, and systemic comorbidities	Likelihood of having a DNAR order in the older age group did not adjust for other factors such as comorbidities or functional status. The study only compared patients ≥80 years with those <80 years

Note. DNR = do not resuscitate; DNAR = do not attempt resuscitation; CPR = cardiopulmonary resuscitation; ICU = intensive care unit; DPAHC = durable power of attorney; AD = advanced directive.

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