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Interventions to Promote End-of-Life Conversations: A Systematic Review and Meta-Analysis

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Abstract

Context

Although several interventions aimed to promote end-of-life conversations are available, it is unclear whether and how these affect delivery of end-of-life conversations. Measuring the processes associated with high-quality end-of-life care may trigger improvement.

Objectives

To estimate the effect of interventions aimed to promote end-of-life conversations in clinical encounters with patients with advanced chronic or terminal illness or their family, on process indicators of end-of-life conversations.

Methods

Systematic review with meta-analysis (PROSPERO no. CRD42021289471). Four databases (PubMed, CINAHL, PsycINFO, and Scopus) were searched up to September 30, 2021. The primary outcomes were any process indicators of end-of-life conversations. Results of pairwise meta-analyses were presented as Risk Ratio (RR) for occurrence, standardized mean difference (SMD) for quality and ratio of means (ROM) for duration. Meta-analysis was not performed when fewer than four studies were available.

Results

A total of 4,663 articles were scanned. Eighteen studies were included in the systematic review and 16 entered at least one meta-analysis: documented occurrence (n = 8), patient-reported occurrence (n = 4), patient-reported-quality (n = 4), duration (n = 4). There was significant variability in settings, patients' clinical conditions, and professionals. No significant effect of interventions on documented occurrence (RR 1.54, 95% CI 0.84–2.84; I^2 91%), patient-reported occurrence (RR 1.52, 95% CI 0.80–2.91; I^2 95%), patient-reported quality (SMD 0.83, 95% CI −1.06 to 2.71; I^2 99%), or duration (ROM 1.20, 95% CI 0.95–1.51; I^2 65%) of end-of-life conversations was found. Data on frequency were conflicting. Interventions targeting multiple stakeholders promoted earlier and more comprehensive conversations.

Conclusion

Heterogeneity was considerable, but findings suggest no significant effect of interventions on occurrence, patient-reported quality and duration of end-of-life conversations. Nevertheless, we found indications for interventions targeting multiple stakeholders to promote earlier and more comprehensive conversations.

Key Words: Clinical encounter; conversations; end of life; meta-analysis; systematic review; terminally ill.

Key Message

This systematic review with meta-analysis found no significant effect on process indicators of interventions aimed to promote end-of-life conversations in clinical encounters with patients with advanced chronic or terminal illnesses or their family. Heterogeneity was considerable and further investigation into their implementation as a collaborative, person-centered effort is warranted.

Introduction

High-quality end-of-life care relies on optimal treatment of symptoms and psychosocial, spiritual and existential support for both patient and family,[1,2] and on knowledge of patients' care preferences to deliver care aligned with their preferences. This requires effective and regular communication such as in advance care planning (ACP) conversations and shared decision-making.[1,2]

Engagement in end-of-life conversations by patients or family, measured in different ways,[3] varies significantly: from 18%[4] to 73%[5] in cancer to 9.5% up to 70% in nursing home settings.[6,7] Indeed, how end-of-life conversations are being defined varies across studies,[8] and adopting a broad definition may be reasonable.

Over the last 30 years, investments have been made to develop resources, strategies and conceptual frameworks for improving end-of-life conversations.9, 10, 11, 12, 13 However, social and healthcare professionals (hereafter professionals)-led end-of-life conversations are still suboptimal from the perspective of both patients and their family.[14] Their measurement based on quality standards represents a milestone and indicators have been identified at the level of physical environment, process, and outcome.[15,16] In serious illnesses, the conversation process mediates goal-concordant care,[17] which constitutes a priority outcome in palliative care.[18] Therefore, measuring this process is critical to ensure high-quality conversations and improve the care provided. Process indicators offer objective and straightforward measures on how care is delivered and can be tracked and easily targeted in interventions aimed to improve the quality of care.[19,20] National consensus bodies recommend ameliorations in the way end-of-life conversations are delivered with respect to their occurrence, quality, timing, frequency, and duration.21, 22, 23, 24

Several international palliative care guidelines recommend accurate documentation of end-of-life conversations in the clinical record not limited to their occurrence.[25] Terminally-ill patients who report any end-of-life communication have better quality of death compared to patients who do not[26] and the quality of dying improves as the quality of conversations increase.[27] High-quality end-of-life communication has been associated with improved outcomes for patient and family,[4,8,28] while absent, late, or poor professionals-patient/family communication contributes to aggressive, lower-quality and patients' non-preferred treatment.[3,29] The "Conversation ready" framework for improving end-of-life care assumes that the quality of documentation depends on the effectiveness and reliability of patients and families engagement, and therefore it can be employed as a basic process measure.[30]

There is widespread support for the need to start end-of-life conversations early in the disease trajectory to give patients and family support, promote preparedness for the upcoming worsening, and offer the opportunity to raise questions with professionals to sustain understanding and involvement of patients in making care decisions.[25] Unfortunately, conversations usually take place late in the disease trajectory with professionals newly involved in the patient's care, and difficult decisions are made in the heat of the moment.[5] One-third of conversations usually take place within one month of death.[31]

A series of conversations may be needed to promote understanding and shared decisions by making information more digestible and allowing processing time.[32] When end-of-life conversations are held on an ongoing basis, they strengthen trust and rapport, and favor the elicitation of personal values and goals and their revisit as the patient's conditions change.[33] Also, family satisfaction increases with frequency[34,35] of conversations and more frequent contact is associated with not providing aggressive care.[36]

Finally, it is recommended to arrange adequate time for conversation to allow patients and families to ask questions and express their views without feeling rushed into a decision.[32,37] Family satisfaction increases when professionals take the time to listen,[38] but end-of-life conversations are often brief.[38,39]

Several interventions aimed to promote end-of-life conversations have been developed but there is no review summarizing evidence on their effects on how end-of-life conversations are delivered.

Previous systematic reviews mainly examined effects on communication skills,[40,41] and on patients' or family caregivers' outcomes.[42] Measuring process indicators that may predict high-quality end-of-life care can support quality improvement efforts by identifying areas of amelioration. Therefore, this paper looks at the end-of-life conversations in terms of occurrence, quality, timing, frequency, and duration.21, 22, 23, 24

The interventions aimed to promote end-of-life conversations have been assessed in trials that varied from explanatory, examining effects in ideal circumstances, to pragmatic in usual care conditions.[43] The type of trial is often not stated explicitly. Describing the trial approach informs the applicability of interventions aimed to promote end-of-life conversations.

Therefore, we systematically reviewed the literature and conducted meta-analyses with the primary objective to estimate the effect of interventions aimed to promote end-of-life conversations in clinical encounters with patients with advanced chronic or terminal illnesses or their family on occurrence, quality, timing, frequency, and duration of end-of-life conversations. The secondary objective was to describe trial approaches (explanatory vs. pragmatic).

Method

Design

A systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[44] (Table A1) was performed. The protocol was registered on 6 December 2021 (PROSPERO CRD42021289471).

Search Strategy and Selection Criteria

Searching PubMed and one giant database (e.g., Scopus, Embase) at minimum is recommended for systematic reviews.[45] We searched four databases (PubMed, CINAHL, PsycINFO, and Scopus) on 30 September 2021 from inception. Searches employed controlled vocabularies and free terms, without temporal or language limits. Search strategies were adapted for each database (Appendix 2). The reference lists of included articles were screened manually to identify potentially relevant publications. Also, the PROSPERO register of systematic reviews was searched for ongoing and recently completed reviews.

In the present study, end of life conversation was defined as a clinical interaction engaging professionals and patients with advanced chronic or terminal illness, or their family, and aimed to promote patient and/or family understanding of illness progression or care options, or elicit patient's care preferences at the end of life.[13] Studies were included if they 1) covered at least one element of this definition; 2) involved adults with advanced, progressive, incurable conditions approaching the end of life[15] and/or their family. Studies involving only family caregivers were also eligible; 3) were intervention studies (i.e., pre post studies, clinical trials, controlled clinical trials, and randomized controlled trials) aimed to promote end-of-life conversations in clinical encounters, regardless the clinical setting and people targeted (i.e., patients, family caregivers, and/or professionals); 4) reported on the effect of interventions on at least one process indicator of end-of-life conversations (i.e., occurrence, quality, timing, frequency, or duration); and 5) were published in peer reviewed journals.

We excluded studies on interventions which targeted the general public or older people more generally (e.g., health campaign, public health initiatives, and policy), or were part of multi-faceted programs and the effect of the individual component of the intervention that related to end-of-life communication was not clearly recognizable and assessable.

As we focused on process outcomes, studies only assessing the impact of interventions on family-related (e.g., psychological distress) or patient-related outcomes (e.g., hospitalizations) were also excluded. Patient/family care outcomes represented additional data that were extracted for descriptive purposes, when available.

Article Screening and Study Selection

S.G. and Y.A. independently screened titles and abstracts, removed duplicates, and reviewed the full text of potentially relevant articles, and discussed any disagreement or uncertainty regarding eligibility until reaching consensus.

Quality Assessment

S.G. and Y.A. assessed study quality using the QualSyst tool for quantitative research.[46] This 14-item tool scored whether specific criteria were met ("fully" = 2, "partially" = 1, "not at all" = 0). Items not relevant for a particular study design were excluded from the summary score that was calculated for each paper and allowed for direct comparison of studies with different designs. Studies were classified as high (>0.9), moderate (0.7-0.9) or low quality (<0.7).

Applicability Assessment

Trial approaches vary from explanatory, examining effects in ideal circumstances, to pragmatic when applicability of the intervention in usual care across a range of settings is relevant.[43] The approach becomes more explanatory as it moves away from usual practice towards ideal circumstances, offering insights in whether the intervention could work at all.

S.G. and Y.A. independently assessed applicability using the PRagmatic Explanatory Continuum Indicator Summary-2 (PRECIS-2) tool,[43] which focuses on trial design choices and comprises nine domains: 1) eligibility criteria; 2) recruitment; 3) setting; 4) organization (expertise and resources to deliver the intervention); 5) flexibility-delivery of intervention; 6) flexibility-measures to ensure adherence to the intervention; 7) follow up; 8) primary outcome; and 9) primary analysis. Each domain was scored on a 5-point scale (1 = very explanatory to 5 = very pragmatic). With insufficient information, we assigned a score of three.

A mean score across studies for each domain and a mean applicability rating for each study were calculated. Domains and studies were classified as mostly explanatory (<4) or mostly pragmatic (≥4) according to the mean domain score and the mean applicability rating, respectively.

Data Extraction

Data were entered into a standardized spreadsheet under the following headings: study characteristics; sample characteristics; narrative summary of findings; and quantitative results (number and proportion of individuals with self-reported or documented occurrence of end-of-life conversations in medical record; mean values (standard deviation [SD]) of patient-reported quality and duration of end-of-life conversations). S.G. and Y.B. independently extracted all data, and solved disagreements by consensus with P.DG.

Primary Outcomes

The primary outcomes were process indicators of end-of-life conversations: occurrence, quality, timing, frequency or duration. Occurrence: the proportion of patients reporting, or with documented conversations. Quality: the quality of conversations either perceived by patients, family caregivers, or professionals, or according to their thematic content. Timing: time before death. Frequency: number of conversations per patient irrespective of the timing. Duration: length of conversations. Occurrence was expressed as percentage, quality as mean (SD) for quantitative measures (e.g., quality of care item) or thematic domains of conversations (e.g., values and goals, prognosis) for qualitative measures, timing as mean or median, frequency and duration as mean.

Data Analysis and Synthesis

Interventions were categorized into those targeting patients, professionals, or multiple stakeholders, and according to system level strategies e.g., alerts, electronic documentation template, and the number of sessions (one-time vs. multiple-sessions interventions).

We used prevalence ratios for occurrence, standardized mean difference (SMD) for patient-reported quality and ratio of means (ROM) for duration of end-of-life conversations. A random-effect model meta-analysis with unrestricted maximum likelihood using the sample size as a weighting factor was performed when any of the primary quantitative outcomes was assessed in at least four studies. Hartung-Knapp method was applied.[47] Heterogeneity was assessed using the Cochran Q test via a Mantel-Haenszel test and quantified by I^2 statistic.[48] Subgroup analyses with random-effects models investigated the association between documented occurrence and persons targeted, system strategies, and number of sessions. Sensitivity analyses for outliers were also performed.
Funnel plots were used for publication bias. Results were considered statistically significant at 2-tail $P < 0.05$. R v 4.1.2 was used for all analyses.

Results

Review Process

A total of 4,663 articles were identified; 32 full texts remained after screening titles and abstracts. Seventeen were excluded (Table A2). Three additional articles were identified from reference lists; thus 18 studies were included (Fig. 1). These assessed five process outcomes: occurrence,[31,]49, 50, 51, 52, 53, 54, 55, 56, 57, 58 quality,[49,50,52,53,55,56,]58, 59, 60, 61, 62, 63 timing,[31,55,58] frequency,[31,55] and duration62, 63, 64, 65 of end-of-life conversations (Table 1 and 2). Two articles could not be included in any meta-analyses: one[60] did not quantify the quality of conversations, and one[61] did not provide overall estimates of changes in the patient-reported quality of conversations.

Characteristics of Included Studies

Thirteen[31,]49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60 studies were conducted in the United States, two[62,63] in Australia, one[64] in the Netherlands, one[65] in France, and one[61] in Japan; all but two[51,57] were published after 2005. Ten49, 50, 51, 52[,55,59,60,]63, 64, 65 studies were classified as high, five[31,53,56,57,62] as moderate and three[54,58,61] as low quality (Table A3).
Thirteen[31,]49, 50, 51, 52[,]54, 55, 56, 57[,61,62,64,65] studies were hospital-based, three[59,60,63] involved both clinics and inpatient services, and two[53,58] only clinics.
Studies involved patients with cancer,50, 51, 52[,]54, 55, 56, 57[,]59, 60, 61, 62, 63, 64, 65 end-stage pulmonary,[31,49,51,52,56,57,59,65] cardiac,51, 52, 53[,56,57,59,65] liver,[51,52,59,65] renal,[52,56,57] or metabolic disease,[52,57] or multiple severe comorbidities[51,58,59]. Only one study involved patients with dementia,[56] gastrointestinal,[57] infectious,[57] neurologic,[57] or rheumatologic[57] end-stage disease.
Among professionals, studies most frequently involved oncologists,50, 51, 52[,55,60,]62, 63, 64 or internists[49,51,52,57,59] (Table 1, A4).

Definition of End-of-Life Conversations

In the included studies, end-of-life conversations were defined as discussions, conversations, communications, talks, or information about symptom management,[51,53] treatment plans,[51,53,61] end-of-life care,[57,59,60,63] goals of care,[52,]54, 55, 56[,58] treatment options with their benefits and harms,[54,55,61,62,64] illness trajectory and prognosis,52, 53, 54[,56,58,60,62,63] and patients' values or care preferences[31,]49, 50, 51[,55,56,58,62,64,65] (Table 1).

Interventions to Promote End-of-Life Conversations

In all, 12 unique interventions across 18 studies were identified. The interventions targeted multiple stakeholders (n = 10),[31,49,52,53,55,60,]62, 63, 64, 65 professionals only (n = 7),[50,51,54,]56, 57, 58, 59 or patients only[61]. Four studies[60,62,63,65] involved family caregivers.
Coaching (n = 7),[50,53,55,56,58,60,62] a patient-specific information form about end-of-life care preferences (n = 4),[31,49,51,53] written resources such as question prompts list, information leaflet, communication guide, and communication guidelines or standardized protocols (n = 4),[55,60,]62, 63, 64, 65 videos with

educational or supportive purposes (n = 3),[60,62,64] and a patient-specific communication tips form (n = 2)[52,53] targeted both patients and professionals. Disclosure of more detailed information about clinical conditions[61] and face-to-face meeting[62] targeted only patients. Lectures (n = 6),[50,54,55,57,59,64] role play (n = 6),[50,]57, 58, 59, 60[,64] individual- or small group-based reflective discussions (n = 5)[54,57,59,60,64] provision of a prognostic estimate (n = 1),[51] or palliative care consultation (n = 1)[54] targeted only professionals. Five[51,]55, 56, 57, 58 studies also introduced strategies at the system level. System strategies included email remainders, alerts, or administrative prompts (n = 2),[56,57] an electronic documentation template for conversations (n = 2),[55,58] and a trained nurse who facilitated conversations (n = 1)[51,58]. Eight[31,49,52,53,57,61,63,65] studies assessed one-time interventions while ten[50,51,]54, 55, 56[,]58, 59, 60[,62,64] multiple-session interventions. Interventions were delivered by nurses only,[51,53,62] physicians only,[50,63,65] experienced trainers (undefined qualification),[56,64] or multi-professional teams[43,54,55,57,59,60] (Table 1, 3, and A5).

Outcomes of Interventions Aimed at Promoting End-of-Life Conversations

All funnel plots exhibit asymmetry, as depicted in Figure A1. While asymmetry has traditionally been linked to publication bias and selective outcome reporting, it can also be caused by heterogeneity. Methodological differences can contribute to heterogeneity, with smaller studies,[53] lower quality studies,[54,58] or studies with mostly explanatory design[52,53] tending to show larger effects. This is supported, in Figure A1, by studies reporting large effects also have larger standard errors.

Occurrence

Ten studies assessed documented occurrence of end-of-life conversations: eight[31,]52, 53, 54, 55, 56, 57, 58 in clinical records, two[55,58] in a specific module of the electronic clinical record, and four49, 50, 51, 52 patient-reported occurrence. Seven of eleven[49,]51, 52, 53, 54, 55[,58] studies showed positive results, four of eleven[31,50,56,57] null results. Among the seven studies with positive results, one[53] had a wide CI with a small sample size and three[51,55,58] showed border-significant CIs.

Eight of eight[31,]52, 53, 54, 55, 56, 57, 58 studies contributed to the meta-analysis of documented occurrence in clinical records, with no significant effect of interventions (RR 1.54, 95% CI 0.84–2.84, I^2 91%) (Fig. 2). Results were similar in sensitivity and subgroup analyses (Fig. A2).

Four of four49, 50, 51, 52 studies indicated no significant effect on patient-reported occurrence (RR 1.52, 95% CI 0.80–2.91, I^2 95%) (Fig. 2).

Quality

Patients’,[49,50,52,53,59,61] family caregivers’[59] and professionals’[59] self-reports, and thematic content[55,56,58,60,62,63] of end-of-life conversations were employed to assess quality. Quality was assessed using the Quality of Communication questionnaire,[49,52,53,59] the Support Team Assessment Schedule-Japanese version,[61] the Numeric Rating Scale 0–10[50] or a composite score of communication measures,[60] or coding the content of conversations in thematic domains.[55,56,58,62,63] Three of six studies[49,52,61] showed positive quantitative results, the other three of six[50,53,59] null results. Only two[49,52] studies with positive results contributed to the meta-analysis. In all, four of six[49,52,53,59] studies contributed to the meta-analysis, which showed no effect on patient-reported quality (SMD 0.83, 95% CI −1.06 to 2.71, I^2 99%) (Fig. 2).

Quantitative evidence showed that interventions targeting only professionals did not improve the quality of conversations perceived by family or professionals.[59] In all, six of six[55,56,58,60,62,63] studies showed positive qualitative results based on the thematic domains of the conversations. Interventions targeting multiple stakeholders were more likely to increase the number of relevant domains (e.g., values/goals, life-sustaining treatment preferences) discussed[55,63] and the time trained professionals addressed them,[56] compared to interventions targeting only professionals.[58] Also, interventions targeting multiple stakeholders increased the number of statements to inform patients about prognosis and treatment choices (+38%), engage patients in conversation (+44%), and respond to patients' emotions (+71%);[60] patients' and their family caregivers' cues and questions about end of life and end-of-life care also increased.[62,63]

Timing

Three[31,55,58] studies assessed timing. Conversations took place earlier when interventions targeted multiple stakeholders (median 143 days)[55] compared to involving only professionals (mean 133 days).[58]

Frequency

Of the two[31,55] studies targeting multiple stakeholders, one[55] highlighted higher frequency of end-of-life conversations (mean 3.1 [95% CI 2.5–3.6] per intervention patient vs. 2.1 [95% CI 1.4–2.8] per control patient, $P = 0.02$), while the other[31] found no difference (mean 3.1 (SD 4.0) vs. 2.6 (SD 3.2), $P = 0.47$).

Duration

Four studies targeting multiple stakeholders assessed the duration of end-of-life conversations.62, 63, 64, 65

Two of four[63,65] studies showed positive results, the others[62,64] null results. Four of four[62,65] studies contributed to the meta-analysis, which showed no effect on duration (ROM 1.20, 95% CI 0.95–1.51, I^2 65%) (Fig. 2).

Patients- and Family Caregivers-Related Care Outcomes

Thirteen of eighteen studies assessed the impact of interventions on outcomes [50,54,56,59,60,]62, 63, 64, 65 (Table A6).

Four[54,56,59,65] studies (three[54,56,59] targeting professionals only and one[65] multiple stakeholders) found significant changes with mixed results: decrease in overall ($P < 0.001$) and 30-day readmission rates ($P = 0.009$) with improvement of the content without changes in the occurrence of conversations;[56] increased occurrence of conversations in clinical records with increased palliative care consultation ($P = 0.026$) but reduced screening of constipation ($P = 0.041$);[54] decreased patients' post-traumatic stress disorder ($P = 0.01$), anxiety ($P = 0.02$), and depression ($P = 0.003$) with longer conversations;[65] increased patients' depression ($P = 0.006$) without improvement in patient, family caregivers, or clinician-reported reported quality of conversations.[59]

Four[31,51,53,57] studies assessed the impact of interventions on advance directives and one[56] on ACP. No difference in completion of advance directives neither in documented ACP was found.

Applicability of the Interventions

Fourteen[31,]49, 50, 51,54, 55, 56, 57, 58,61, 62, 63, 64, 65 studies were mostly pragmatic, four[52,53,59,60] mostly explanatory. Among the domains of PRECIS-2 tool, eligibility criteria, recruitment modalities, flexibility in engagement, primary outcome, and primary analyses were mostly pragmatic. Setting, expertise and resources needed, flexibility in the delivery, and follow up were mostly explanatory (Table A7).

Discussion

Our systematic review on end-of-life conversations found interventions were mostly pragmatic with no effect on the occurrence, patient-reported quality or duration of conversations, regardless of who was targeted, the introduction of system strategies, or the number of sessions. The meta-analyses showed high heterogeneity likely due to wide variability in contexts, patients' clinical conditions, and interventions delivered. However, qualitative and quantitative evidence indicated that when interventions targeted multiple stakeholders, conversations were earlier and more comprehensive (e.g., number of relevant domains addressed or information about prognosis and treatment choices), regardless of the strategies employed;[55,60,62] unfortunately, these positive results could not be tested in meta-analyses to ascertain significant differences for the lack of power. Instead, the effect of interventions on frequency[31,55] was limited and conflicting.

Process indicators of occurrence, quality, timing, frequency, and duration provide clear and objective measures on how end-of-life conversations are delivered, and comply with the evaluation criteria of reliability, validity, responsiveness to change, and ease of implementation to effectively guide quality improvement efforts.[19,20]

Documented occurrence of conversations in clinical records was the most frequent process outcome,[31,]52, 53, 54, 55, 56, 57, 58 followed by patient-reported quality,[49,50,52,53,59,61] and thematic content of conversations.[55,56,58,60,62,63] This may reflect recommendations in most international palliative care guidelines to clearly document conversations and their content.[25] Tracking what has been discussed, it is helpful to put at the front elements of shared decision-making such as the patient's understanding of illness and end-of-life care options, and their values and care preference.[66] Unfortunately, several domains of conversations relevant to direct end-of-life care are poorly discussed: only half of the conversations covers psychological problems and less than 40% addresses spiritual and existential issues.[6] Also, options in terms of palliative care are not discussed at all in 45% of conversations.[6] Measuring the process rather than measuring only the final outcome -advance directives completion- that is often the result aimed for, allows to verify if the care goals are consistent with the patient's stated preferences. A multidisciplinary expert panel ranked consistency between documented care goals and the patient's stated preferences as the most important of a list of quality indicators for documentation of end-of-life communication and decision-making.[13]

Also, there is consensus that such information should be easily accessible by professionals within and beyond the current team involved in the care and cover conversations that have taken place at any time point over the disease trajectory.[67] Care for adults nearing the end of life is indeed coordinated by health and social care professionals in various services and organizations that would benefit from knowing about any conversations about prognosis, treatment goals, and care plans.[15] To support that patients' wishes are honored, it is crucial that the documentation is easily accessible.[68,69] A structured, specific module on end-of-life conversations in the electronic clinical record may promote greater accessibility, and be used to monitor the effect of an intervention on process indicators of conversations, such as timing, frequency, and key content. Only two[55,58] studies in our review assessed documented occurrence in a specific module of the electronic medical record, suggesting that despite the potential of this process measure, it is still at its dawn and likely linked with the features of the local healthcare information system.

The timing of a conversation is another key process indicator to be monitored. Evidence of benefit is accumulating on initiating conversations well before the last days of life.[70] However, end-of-life conversations are hindered by several obstacles and interventions targeting only professionals may not be enough. When interventions target multiple stakeholders, they work at multiple levels by reducing professionals' uncertainties about the right time to start conversations and simultaneously increasing patients' and family caregivers' question-asking about end-of-life care,[62,63] that was found to play an essential prompting role.[71]

End-of-life conversations should allow adequate time to process and digest the information that are given.[32] Being in a rush is a well-known obstacle to conversations and professionals are recommended to take the time to listen to patients and create the conditions to help the conversation run smoothly.[72] In settings such as the nursing homes where stays are usually long and patients and family are familiar with the professionals, brief but more frequent encounters that break information into multiple chunks may work better to promote understanding and, finally, shared decision-making.

Our meta-analytic findings suggest no overall effect of the interventions on any process indicators of conversations despite several positive individual study outcomes. The high heterogeneity may be responsible for these null results. Unfortunately, there was not enough power for subgroup analyses to explore whether results differed for groups such as whom was targeted, employment of system level strategies, number of sessions, setting, family involvement, and trial design. However, visual inspection of the meta-analyses plots shows that subgroups of studies have the same clear and positive direction of the intervention effect. Particularly, in the plot of documented occurrence, two[52,53] explanatory studies found the intervention to be effective while the effect was unclear or border-significant in pragmatic studies.[31,]54, 55, 56, 57, 58 This suggests that the interventions have best chances to demonstrate a beneficial effect in ideal settings, while implementation in real care circumstance needs improvement. In the plot of patient-reported occurrence, interventions targeting multiple stakeholders[49,52] reported greater effect compared to interventions involving only professionals.[50,51] This prompts more situational awareness that serves better understanding of illness and prognosis.

Regardless of limited effects on communication process indicators, the interventions may have taught professionals what issues to discuss[73] and possibly improved their sensitivity to addressing emotions.[60] Such skills need time and practice to develop, therefore these interventions may not immediately result in improved patient-reported quality of conversations. Moreover, training was often a few hours, one-time55, 56, 57[,64] or over a few weeks.[50,60] Link of interventions to outcomes was not an objective of the study, but unchanged anxiety[52,53,63,65] and increased depression only in one study[59] should reassure professionals that conversations about the end of life may be emotional but probably not harmful, and encourage them to engage in such conversations.[52,53,63]

The setting of interventions is a further recognized measure to assess the quality of care that needs to be considered.[17] Only five[53,]58, 59, 60[,63] studies involved out-of-hospital settings (i.e., heart failure, primary care, palliative care or cancer clinics). However, the way health care is being delivered is changing; developed countries are adopting community-centered approaches and boosting out-of-hospital care.74, 75, 76 Moreover, increasing care transitions in the late stages of illness may be avoided by primary care teams as better positioned to initiate and conduct regular end-of-life conversations to guide continuous care.[77] None of the studies were conducted in nursing homes, which is, among the out-of-hospital settings, at the frontline of caring for frail older people at the end of life and their family.[78] Only one[56] study involved patients with dementia and only in three[60,62,65] studies the intervention targeted family caregivers. When family caregivers are involved in end-of-life conversations, the likelihood to limit or withdraw life-sustaining treatments increases and it facilitates transitioning toward palliative-oriented care.[8,79] Interventions to promote end-of-life conversations should be introduced and tested in particular in community settings and involve family caregivers.

Strengths and Limitations

Our findings should be read considering the lack of a common definition of end-of-life conversations, although this offers a picture of current practice. Second, documented occurrence of conversations may not reflect actual discussions or the provision of goal-concordant care. However, the outcomes were informed by several sources of information, including patients', family caregivers' or professionals' questionnaires or interviews, and videotaped or audio-recorded consultations in addition to medical records, in an effort to capture the nuances and content of end-of-life conversations beyond a simple binary outcome of occurrence. Third, we did not collect data about professionals' communication skills which are critical to establish trusting relationships that in turn may affect process and care outcome.[79] Last, we did not have enough power to explore the subgroup effects of interventions aimed to promote end-of-life conversations in a specific setting or when family was involved.

Conclusions

This systematic review and meta-analysis found no effect of interventions aimed to promote end-of-life conversations on occurrence, quality, timing, frequency and duration of these conversations. Nevertheless, we found indications for interventions targeting multiple stakeholders to promote earlier and more comprehensive conversations; future study should identify effective elements.

Overall, studies were mostly pragmatic even if settings involved, resources, flexibility in delivering the intervention and follow up modalities were mostly explanatory. This suggests implementation of interventions can be improved. Considerable heterogeneity renders conclusions tentative. Future research should examine the effect of interventions aimed to promote end-of-life conversations by employing standardized process indicators that represent the natural, basic starting point of evaluation to elicit implementation challenges or failure, and trigger improvement.

Author Contributions

BA, JTS, PB, PDG, SG, VD, and YA. For the purposes of authorship, Prof. Di Giulio and Prof. van der Steen contributed equally. Dr Gonella had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization: Di Giulio, Dimonte, Gonella. Methodology: Di Giulio, Gonella, van der Steen. Software: Berchialla. Validation: Gonella. Formal analysis: Berchialla. Investigation: Arnone, Gonella. Resources: Arnone, Gonella. Data curation: Gonella. Writing—Original draft: Di Giulio, Gonella, van der Steen. Writing—Review & Editing: Albanesi, Arnone, Berchialla, Dimonte. Visualization: Gonella. Supervision: Di Giulio, van der Steen. Project administration: Gonella.

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Table 1. Characteristics of Included Studies

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics							Main Findings
								Patients		Family Members	Professionals				
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator(s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting/ Size (N)	Underlying Disease	Life Expectancy (m)	(N) Males (%) Age, years	(N) Males (%) Age, Years	Professional Profile	Working Experience, Years[a]		
Au et al. (USA, 2012) High Mostly pragmatic	Cluster RCT / January 2004 to November 2007	Discussions about preference for EoL care	I: an individualized patient-specific feedback form based on a previous patient's survey about preference for EoL care was provided to physicians (n = 42) and their patients (n = 194) C: no patient-specific feedback for neither physicians (n = 50) nor patients (n = 182)	NA	**Patient-Reported Quality of EoL Conversations** Proportion of patients reporting occurrence of conversation about EoL preferences between patients and their physician or their surrogate	Patients' questionnaire (baseline and two weeks after the clinic visit)	Two hospitals / Not reported	N = 376 Chronic obstructive pulmonary disease	Not reported	-	N = 92 I: 42 M: 21 (50) Age: Not reported C: 50 M: 22 (44) Age: Not reported	Internists, lung specialists, geriatricians	Not reported		1) **Improved Quality of EoL conversations Assessed with the QoC Questionnaire 0−100 in the Intervention Group** (Adjusted difference 5.74 points, p = 0.03, Cohen effect size = 0.21); 2) More intervention patients reporting EoL conversations with their clinicians (Adjusted difference 27.4%, *P* < 0.001); 3) More intervention patients reporting EoL conversations with their surrogate (Adjusted difference 10.9%, p < 0.01).
Bickell et al. (USA, 2020) High Mostly pragmatic	Cluster RCT / Not reported	Conversations on eliciting patient values about care and treatments	I: physicians received a 2-hour small group role play session+4 coaching visits (n = 11) C: no training (n = 11) All intervention and control physicians attended a didactic lecture about the importance of conducting EoL discussions	Physician	**Proportion of patients reporting occurrence of EoL conversations** **Proportion of patients reporting high-quality EoL conversations**	Patients' questionnaire (within days after the clinic visit and at 6 months)	Three hospitals / Not reported	N = 265 Advanced cancer	< 24	-	N = 22 I = 11 M: 7 (64) Age: 44.3 (8.9) C = 11 M: 8 (73) Age: 43.5 (10.7)	Oncologists	I: 17.3 (Not reported) C: 17.0 (Not reported)		1) **No difference in the occurrence of EoL conversations in intervention patients compared to control patients** (52% vs. 48%, OR 0.98, 95% CI, 0.95 −1.01); 2) **No difference in the occurrence of high-quality EoL conversations (scores of 9−10 on NRS 0−10) in intervention patients compared to control patients** (62% vs. 67%, *P* = 0.37); 3) No difference in the composite score of occurrence or quality of EoL conversations in intervention patients compared to control patients (Adjusted OR 0.84, 95% CI 0.57−1.23); 4) At 6 months, no difference in the mean number of emergency department visits and hospitalization, median time between hospice enrollment and death, chemotherapy administration, and intensive care unit admission.

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics						Main Findings
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator (s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting/ Size (N)	Patients Underlying Disease	Life Expectancy (m)	Family Members (N) Males (%) Age, years	Professionals (N) Males (%) Age, Years	Professional Profile	Working Experience, Years*	
Clayton et al., (Australia, 2007) High Mostly pragmatic	Parallel-group RCT / October 2002 to August 2004	Discussions about prognosis and EoL issues	I: patients (and their family caregiver if present) were given a question prompt list 20–30 minutes before their consultation with the physician; physicians were asked to actively endorse and refer to the question prompt list using a standardized protocol (n =92) C: usual consultation (n = 82)	Physician	**Count of overall questions,** questions for palliative care service, physical symptoms, treatment, prognosis, quality of life, support, concerns about professional care, caregiver and EoL issues and **for patients** and their family caregivers Total number of items discussed Duration of consultation	Audio-recorded consultations	Nine palliative care services (mostly outpatient clinics) / Not reported	N = 174 Advanced cancer	Not reported	N = 123 I: 70 M: NR Age: NR C: 53 M: NR Age: NR	N = 15 M: Not reported Age: Not reported	Palliative care physicians	Not reported	1) **More overall questions** ($P < 0.0001$), questions about palliative care service ($P < 0.0001$), prognosis ($P = 0.004$), quality of life ($P < 0.0001$), and support ($P < 0.0001$) **in intervention patients;** 2) More overall questions ($P = 0.0005$), questions about palliative care service ($P = 0.03$), prognosis ($P = 0.05$), and caregiver issues ($P < 0.0001$) in intervention family caregivers; 3) Overall, 23% more items discussed during consultations with intervention patients compared to control ($P < 0.0001$); 4) Increased consultation duration (37.8 minutes in the intervention group vs. 30.5 minutes in the control group, ratio 1.24 95% CI 1.09–1.41); 5) No difference in patients' anxiety, their satisfaction with communication and overall measures of achievement of information needs at 24 hours and 3 weeks.
Connors et al., (USA, 1995) High Mostly pragmatic	Cluster RCT / January 1992 to January 1994	Discussions to elicit preferences, improve understanding of outcomes, encourage attention to pain control, and facilitate planning for future decisions	I: physicians received prognostic information and patient preferences for EoL care. A skilled nurse had multiple contacts with the patient, family, physician and hospital staff to elicit and document preferences, improve understanding of outcomes, encourage attention to pain control, and facilitate planning for future decisions C: usual care	Nurse	Proportion of patients reporting occurrence of EoL conversations	Patients interview or family caregivers interview when patient interview was not possible (between days 2 and 7 and again between days 6 and 15 after study enrollment)	Five hospitals / Not reported	N = 4804 Oncologic, pulmonary, cardiac and liver end-stage disease, coma, or multiple organ system failure with sepsis	Not reported	-	N = 27 physician's specialty groups I: 16 physician specialty groups C: 11 physician specialty groups	Internal medicine, pulmonology/ medical intensive care unit, oncology, surgery, and cardiology	Not reported	**1) No difference in the prevalence or timing of documented DNR orders** (Adjusted ratio of median time 1.02, 95% CI 0.90–1.15); 1) No difference in the proportion of intervention patients or family caregivers reporting discussed cardiopulmonary resuscitation preferences compared to control patients (40% vs. 37%); 2) No difference in the median days spent in intensive care units, comatose, or receiving mechanical ventilation, neither in moderate to severe self-reported pain during the five yrs study period.

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics						Main Findings
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator(s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting / Size (N)	Patients Underlying Disease	Life Expectancy (m)	Family Members (N) Males (%) Age, years	Professionals (N) Males (%) Age, Years	Professional Profile	Working Experience, Years°	
Curtis et al. (USA, 2013) High Mostly explanatory	Cluster RCT / October 2007 to January 2013	Discussions about palliative and EoL care	I: physician and nurse trainees received eight 4-hour sessions including overview didactic with demonstration role-play, simulation and reflective discussions (n = 211) C: usual education (n = 234)	Physician Nurse	**Patient-reported quality of EoL conversations** **Family caregiver-reported quality of EoL conversations** **Clinician-reported quality of EoL conversations**	Patients, family caregivers and clinicians surveys (during the 6-month period preceding intervention and in the 10 months following the intervention)	Primary care clinics and inpatient services / Not reported	N = 1717 Oncologic, pulmonary, cardiac or liver end-stage disease, or multiple severe comorbidities	12 to 24	N = 898 I: 412 M: 106 (26) Age: 56.8 (13.7) C: 486 M: 124 (26) Age: 56.6 (13.5)	N = 445 I: 211 M: 91 (43) Age: 30.5 (5.8) C: 234 M: 98 (42) Age: 30.3 (4.8) Clinicians evaluators N = 890	Internal medicine residents and nurse practitioner trainees	I: median 1.0 IQR (1-2) C: median 1.0 IQR (1-2)	1) Comparing intervention to control, **no difference in reported quality of EoL conversations on the QoC questionnaire score (0 – 10) for patient** (Adjusted b 0.38, 95% CI −0.14 to 0.90, $P = 0.15$); **family caregiver** (Adjusted b 0.11, 95% CI −0.77 to 0.98, $P = 0.81$); and **clinician** (Adjusted b 0.19, 95% CI −0.08 to 0.47, $P = 0.17$); 2) No association between the intervention and patients' physical and mental status, or family caregivers' depression score; increased depression among intervention patients ($P = 0.006$).
Curtis et al. (USA, 2018) High Mostly explanatory	Cluster RCT / February 2014 to May 2016	Talks with patients about their prognosis or goals of care	I: a patient-specific 1-page communication tips based on a previous survey was sent to patients (n = 249) and clinicians (n = 65) one week and 1 or 2 working days prior to the clinic visit, respectively C: patients completed the same survey but no information was provided to patients (n = 288) or clinicians (n = 67)	NA	**Proportion of patients reporting occurrence of EoL conversations** Proportion of patients with documented occurrence of EoL conversations Patient-reported quality of EoL conversations	Patients' questionnaire (two weeks after the clinic visit) Electronic medical record review (from the clinic visit through the following 6 months)	Seven hospitals, one cancer center, two outpatient network / Not reported	N = 494 Oncologic, pulmonary, cardiac, liver renal, or metabolic end-stage disease	<24	-	N = 124 M: 58 (46.8) Age: 47.2 (9.6) I = 59 M: Not reported Age: Not reported C = 65 M: Not reported Age: Not reported	Family medicine, internal medicine, oncology, pulmonology, cardiology, gastroenterology, nephrology, geriatrics	Not reported	1) **More intervention patients reporting occurrence of EoL conversations** (74% vs. 31%, Adjusted β 1.25 [95% CI 0.94-1.56], $P < 0.001$); 2) More intervention patients with documented EoL conversations (62% vs. 17%, Adjusted β 1.25 [95% CI 0.92-1.58], $P < 0.001$); 3) Higher mean quality of EoL conversations assessed with the QoC questionnaire (a priori selection of 4 items rated from 0 to 10) in intervention patients (4.59 vs. 2.13, Adjusted β 2.02 [95% CI 0.48-3.57], $P = 0.01$); 4) No difference in depression or anxiety at 3 and 6 months.
Parallel-group RCT / two-yrs period	Discussions about illness trajectory, prognostic estimates, symptom		management, and advance care planning	I: patients received nurse-led telephone-based previsit coachings+ one-page patient activation outline constructed during the call and shared with both the patient and their physician	Nurse	**Proportion of patients with documented occurrence of EoL conversations** Patient-reported quality of EoL conversations	Patients' questionnaire and electronic medical record review (baseline and two weeks after the clinic visit)	One heart failure outpatient clinic / 600 patients each year	N = 80 Heart failure	Not reported	-	-	-	-

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics						Main Findings
										Family Members	Professionals			
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator(s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting / Size (N)	Patients Underlying Disease	Life Expectancy (m)	(N) Males (%) Age, years	(N) Males (%) Age, Years	Professional Profile	Working Experience, Years*	
				along with suggestions for addressing barriers + patient activation, skills enhancement, and role playing conversation openers (n = 41) C: regular visit (n = 39)										1) **More intervention patients with documented EoL conversations** (73% vs. 2.6%, $P < 0.001$); 2) Higher quality of EoL conversations assessed with the QoC questionnaire (0–10) in intervention patients ($P = 0.03$, Cohen effect size = 0.43); 3) No difference in the quality of general conversations between intervention and control patients ($P = 0.76$, Cohen effect size = 0.13); 4) No difference in completion of advance directives between intervention and control patients (16.1% vs. 7.7%, $P = 0.24$); 5) No difference in palliative care referral, depression, and anxiety.

Author (s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics						Main Findings
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator (s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting/ Size (N)	Patients Underlying Disease	Life Expectancy (m)	Family Members (N) Males (%) Age, years	Professionals (N) Males (%) Age, Years	Professional Profile	Working Experience, Years¹	
Epstein et al. (USA, 2017) High Mostly explanatory	Cluster RCT / August 2012 to October 2015	Discussions about disease course, prognosis, treatment decisions and EoL care	I: oncologists received a two-sessions in-office training (1.75 hours) using a brief video and feedback from standardized patients portraying roles of patients +focused learner-centered reflective feedback. Patients and their caregivers received a single one-hour coaching session incorporating a question prompt list +up to 3 follow-up phone calls in the next 3 months. C: no training	Nurse Social worker	**Composite measure of quality communication** (z scores of engaging patients in consultation [Active Patient Participation Coding], responding to patients' emotions [Verona VR-CoDES], informing patients about prognosis and treatment choices [Prognostic and Treatment Choices [PTCC] Informing subscale], and balanced framing of decisions [PTCC Balanced Framing subscale])	Audio-recorded consultation (after the first training session)	Community-based cancer clinics, academic medical centers and community hospital / Not reported	N = 265 Advanced cancer	< 12	N =194 M: Not reported Age: Not reported	N = 38 I = 19 M: 12 (63) Age: 43.9 (10.3) C = 19 M: 15 (79) Age: 45.3 (9.8)	Oncologists	Not reported	1) **Improved patient-centered communication in the intervention group** (Adjusted δ 0.34 [95% CI 0.06–0.62], P = 0.02) corresponding to 5.7 additional "engaging" statements (+44%), 0.6 additional responses to emotion (+71%), and 1.4 additional statements regarding prognosis and treatment choices (+38%)); 2) No difference in quality of life and aggressive care.
Hanson et al. (USA, 2017) Low Mostly pragmatic	Pre-post study / July 2015 to May 2016		Communication between the patient or patient surrogate and a treating physician or advanced practice provider, with content covering some of the following: treatment goals and values, prognosis, cancer treatment choice, life-sustaining treatment choices, or hospice or comfort care options.	I: residents, medical students, nurse practitioners, and physicians assistants received monthly 45-minute communication skills training (didactic +group discussion) for 10 months +monthly triggered specialty palliative care consultation for 8 months	Nurse Physician Social worker	**Proportion of patients with documented occurrence of EoL conversations**	Medical record review / Not reported	Medical oncology unit of a 804-bed university hospital	N = 172	Advanced cancer	Not reported	-	-	-

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics							Main Findings
								Patients		Family Members	Professionals				
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator(s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting / Size (N)	Underlying Disease	Life Expectancy (m)	(N) Males (%) Age, years	(N) Males (%) Age, Years	Professional Profile	Working Experience, Years*	
														1) **More patients in the post-intervention cohort with documented EoL conversations compared to the pre-intervention cohort** (48% vs. 29%, P = 0.013); 2) Increased EoL conversations over time in temporal trend analysis (P = 0.009); 3) Significant 15% increase in the rate of palliative care consultation; no difference in screening pain, dyspnea, and nausea, while reduced screening of constipation; no difference in spiritual beliefs assessment, 30-day readmission, and intensive care unit transfer.
Henselmans et al. (The Netherlands, 2020) High Mostly pragmatic	Four parallel arms RCT / 2016 to 2018	Discussions about the benefits and harms of the available option as well as the patient's values and preferences	Physicians' 10-hour training consisted of a reader, two group sessions (videos+role play), an individual booster session with personal feedback on a videotaped consultation, and a consultation room tool (n = 15). Patients (n = 97) received a patient communication aid (a paper brochure +question prompt list+value clarification methods) Group A: no physician training +no patient aid (n = 49) Group B: no physician training +patient aid (n = 50) Group C: physician training+ no patient aid (n = 48) Group D: physician training+ patient aid (n = 47)	Experienced trainer	Duration of consultation	Videotaped consultation	Seven hospitals / Not reported	N = 194 Advanced cancer	< 12	-	N = 31 M: 8 (25.9) Age: 41.5 (9.5) I: 15 M: Not reported Age: Not reported C:16 M: Not reported Age: Not reported	Oncologists	7.7 (9.0)	1) Consultation duration (minutes) of 27.51 (12.06), 30.08 (16.03), 36.27 (14.32), and 31.01 (14.27) in group A, B, C, and D respectively; 2) Increased duration of consultation in trained physicians (b 5.43, 95% CI 1.05 −9.54, Cohen' d 0.36); 3) Unchanged duration of consultation in patients receiving the communication aid (b 1.11, 95% CI −3.28 to 5.45, Cohen' d 0.07); 4) Unchanged duration of consultation when interventions were combined (b 0.95, 95% CI −3.24 to 5.71, Cohen' d 0.06); 5) No effect of any interventions on patients' satisfaction with consultation, patients' uncertainty about medical decisions, and quality of life at three months after consultation.

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics						Main Findings
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator (s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting/ Size (N)	Patients Underlying Disease	Life Expectancy (m)	Family Members (N) Males (%) Age, years	(N) Males (%) Age, Years	Professionals Professional Profile	Working Experience, Years'	
Lakin et al. (USA, 2017) Low Mostly pragmatic	Controlled clinical trial / January 2014 to May 2015	Discussions about prognosis, values, goals, or care preferences	I: clinicians received 2.5 hours role play-based training on the use of a conversation guide +monthly coaching (via telephone, email or in-person) +system changes (i.e., surprise question, electronic documentation template, nurse coordinator was notified about patients at high risk of death within 2 yrs to coordinate conversation timing) (n = 59) C: clinicians received no intervention components except for identification of patients using the surprise question (n = 80)	Palliative care experts	**Proportion of patients with documented occurrence of at least one EoL conversation before death** **Timing of the first documented EoL conversation before death** **Comprehensiveness of EoL conversations** **Proportion of patients with documented occurrence of EoL conversations in the advance care planning module of the electronic medical record**	Electronic medical record review (dead patients)	Fourteen primary care clinics / Not reported	N = 178 Multiple severe comorbidities	< 24	-	I: 59 M: Not reported Age: Not reported C: 80 M: Not reported Age: Not reported	Physicians, nurse care coordinators, social workers	Not reported	1) **More intervention patients with documented occurrence of at least one conversation before death** (62.4% vs. 42.9%, $P = 0.002$); 2) **No significant difference in the timing of the first documented conversation in intervention patients compared to control patients** (mean 133.7d before death vs. 129.2 d, respectively, $P = 0.8197$); 3) **More comprehensive conversations about values and goals in intervention patients compared to control patients** (mean 2.8 elements/patient vs. mean 1.8 elements/patient, $P = 0.0301$); **no differences in the discussion of prognosis, life-sustaining treatments, or EoL planning** 4) **More intervention patients with documented conversation in the advance care planning module of the electronic medical record** (44.4% vs. 3%, $P < 0.001$); 5) No difference in hospice use neither in length of hospice stay.
Lautrette et al. (France, 2007) High Mostly pragmatic	Parallel-group RCT / May 2005 to October 2005	Discussions about patients' wishes aimed to promote understanding about the goals of care and offer support	I: clinicians were asked to follow detailed guidelines for EoL conferences; family caregivers received a bereavement information leaflet (n = 63) C: usual practice (n = 63)	Physicians	Duration of consultation	Clocking of family conference	22 Intensive Care (medical and surgical) Units, 15 in teaching hospital and 7 in general hospitals / median number of bed (IQR) 16 (12-21)	N = 126 Chronic obstructive pulmonary disease, chronic heart failure, cancer, cirrhosis	A few days	N = 126 I: 63 M: 12 (23) Age: median 54 (IQR 46-64) C: 63 M: 17 (30) Age: median 54 (IQR 47-59)	N = Not reported M: Not reported Age: Not reported	Not reported	Not reported	1) Longer family conference in the intervention group than in control (median 30 [IQR 19 –45] minutes vs. 20 [IQR 15 –30] minutes); 2) Lower symptoms of post-traumatic stress disorder ($P = 0.01$), anxiety ($P = 0.02$), and depression (p=0.003) in the intervention group than in control.
Pre-post study / April 2004 to March 2008	Information including disease conditions, therapeutic measures, care procedures, and treatment plans	I: disclosure of more detailed information about cancer according to the baseline level of awareness	Not reported	**Patient-reported quality of communication between patient and family Patient-reported quality of**	**communication between medical professionals Patient-reported quality of communication between patient/family and medical professional**	Patients' questionnaire (before and one week after disclosing information)	Two hospitals / Not reported	N = 73 Advanced cancer	Not reported	-	-	-	-	1) **No improvement in the quality of any communication for disclosed group A patients on STAS-J (0–4);** 2) **Improved communication quality between patients and families, between medical professionals, and between patient/families and medical professionals for both disclosed group B and C patients on STAS-**

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics						Main Findings
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator(s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting / Size (N)	Patients Underlying Disease	Life Expectancy (m)	Family Members (N) Males (%) Age, years	Professionals (N) Males (%) Age, Years	Professional Profile	Working Experience, Years'	
		Group A: disclosure of cancer diagnosis (n = 8) Group B: disclosure of life-threatening disease (n = 25) Group C: disclosure of poor prognosis (n = 40)												**J (0-4)** (*P* = 0.0035, *P* = 0.0062, *P* = 0.0013 and *P* = 0.02, *P* = 0.0082, and *P* = 0.0057, respectively); 3) **No improvement in the quality in any communication in not-disclosed group A and B patients on STAS-J (0−4);** 4) **Improved communication quality between medical professionals and between patients/families and medical professionals for nondisclosed group C patients on STAS-J (0−4).**
Paladino et al. (USA, 2019) High Mostly pragmatic	Cluster RCT / September 2012 to June 2016	Discussions about life-prolonging procedures, patients' broader values, goals, and informed preferences	I: physicians received structured communication guide +2.5 hours skilled-based training program +coaching+system changes (i.e., surprise question, email reminders, electronic documentation template) (n = 48); patients received supporting documents (n = 76) C: physicians received no intervention components except for identification of patients using the surprise question (n = 43); no supporting documents for patients (n = 85)	Palliative care faculty	Proportion of patients with documented occurrence of at least one EoL conversation before death Timing of the first documented EoL conversation before death Comprehensiveness of EoL conversations Frequency of documented EoL conversations Proportion of patients with documented occurrence of EoL conversations in an accessible module of the electronic medical record	Electronic medical record review (after death)	Three oncologic centers/ Not reported	N = 161 Advanced cancer	<24	-	N = 91 M: Not reported Age: Not reported I: 48 M: Not reported Age: Not reported C: 43 M: Not reported Age: Not reported	Oncologists	mean 11.5 (95% CI 9.2-13.8)	1) More intervention patients with documented occurrence of at least one conversation before death (96% vs. 79%, *P* = 0.005); 2) Earlier conversations in the intervention group than in the control group (median 143 [IQR, 71−325] d before death vs. 71 [IQR, 33−166] d, respectively, *P* < 0.001); 3) More intervention patients with documented conversation about values/goals (89% vs. 44%, *P* < 0.001), prognosis / illness understanding (91% vs. 48%, *P* < 0.001), and life-sustaining treatment preferences (63% vs. 32%, *P* = 0.004); no difference in documented conversation about EoL ACP (80% intervention vs. 68% control, *P* = 0.08); 4) Higher comprehensiveness (*P* < 0.001) and frequency (mean 3.1 [95% CI 2.5-3.6] conversation per patient vs. mean 2.1 [95% CI 1.4-2.8] conversation per patient, *P* = 0.02) of documented conversations in intervention patients; 5) More intervention patients with documented conversation in the accessible module of the electronic medical record (61% vs. 11%, *P* < 0.001).

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics						Main Findings
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator(s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting/ Size (N)	Patients Underlying Disease	Life Expectancy (m)	Family Members (N) Males (%) Age, years	(N) Males (%) Age, Years	Professionals Professional Profile	Working Experience, Years*	
Pollak et al. (USA, 2019) Moderate Mostly pragmatic	Cluster RCT / July 2017 to March 2018	Conversations about goals, preference and prognosis that affect treatment decisions	I: physicians received alerts and 2-hour communication coaching provided in 3 sessions (n = 8) C: no training (n = 7)	Communication coach	**Proportion of patients with documented occurrence of EoL conversations** Comprehensiveness of EoL conversations	Medical record review / Not reported	One hospital / Not reported	N = 428 Metastatic cancer, dementia, congestive heart failure, chronic obstructive pulmonary disease, or end-stage renal disease	Not reported	-	N = 15 I: 8 M: 4 (50) Age: 38.5 (4.7) C: 7 M: 5 (71) Age: 34.5 (3.2)	Not reported	Not reported	1) **No difference in documented conversations between intervention and control** (OR 0.97, 95% CI 0.64–1.46, P = 0.8616); 2) Increased percentage of time among trained physicians to address emotions (from 50% to 94%), discuss priorities (from 42% to 88%), elicit understanding of illness from 42% to 75%), discuss prognosis (from 42% to 50%), and make recommendations from 33% to 50%); 3) No difference in documented ACP in intervention compared to control (4.5% vs. 3.8%, OR 2.01, 95% CI 0.96–4.21, P = 0.052); 4) Fewer overall (P < 0.001) and 30-day readmission rates (P = 0.009) in intervention compared to control; no significant difference in length of stay, palliative care referral and hospice referral.
Reinke et al. (USA, 2017) Moderate Mostly pragmatic	Followup study of a cluster RCT / January 2004 to September 2013	Discussions to help patients and surrogate decision makers prepare to make in-the moment decisions based on one's values and preference for care	I: an individualized patient-specific feedback form based on a previous patient's survey about preference for EoL care was provided to physicians and their patients C: no patient-specific feedback for neither physicians nor patients	NA	**Proportion of patients with documented occurrence of at least one EoL conversation before death** Frequency of documented EoL conversation Timing of documented EoL conversation before death	Medical record review (dead patients)	One hospital / Not reported	N = 157 Chronic obstructive pulmonary disease	Not reported	-	-	-	-	1) **No difference in the proportion of patients with documented occurrence of at least one EoL conversation before death between intervention and control** (75% vs. 72%, Adjusted OR = 1.30, 95% CI 0.58–2.92, P = 0.53); 2) **No difference in the odds of completing an advance directive** (OR 1.30, 95% CI 0.614–2.77); 3) Documentation of 451 unique EoL conversations for 115 of 157 (73%) patients; 4) No difference in the mean frequency of documented EoL conversations in intervention patients compared to control patients (mean 3.1 (SD 4.0) vs. 2.6 (SD 3.2), P = 0.47); 5) Occurrence of EoL conversations over 3.6 yrs (range from 9 months to 8.6 yrs); 54 of 157 (34%) EoL conversations conducted within one month of death.

Author(s) (Country, year) Quality Score* Applicability**	Study Characteristics							Study Sample Characteristics						Main Findings
	Design / Study Period	Definition of EoL Conversation	Intervention	Who Delivered the Intervention	Process Indicator(s) of EoL Conversations Investigated	Data Source (Time of Data Collection)	Setting/ Size (N)	Patients Underlying Disease	Life Expectancy (m)	Family Members (N) Males (%) Age, years	Professionals (N) Males (%) Age, Years	Professional Profile	Working Experience, Years*	
Shorr et al. (USA, 2000) Moderate Mostly pragmatic	Pre-post study / pre-intervention cohort February to May 1995; post-intervention cohort April to June 1997	Discussions regarding EoL care and EoL issues	I: Physicians received administrative prompts to encourage EoL conversations and had a mandatory one-day educational seminar on EoL issues based on didactic lectures, small group discussions and role-playing	Ethics committee members	**Proportion of patients with documented occurrence of EoL conversations**	Medical record review / Not reported	One hospital / Not reported	N = 305 Cardiac, pulmonary, gastrointestional, infectious, renal, oncologic, neurologic, rheumatologic, or metabolic end-stage disease	<36	-	N = 115/167 (68.9%) completed the training M: Not reported Age: Not reported	Internists	Not reported	1) **No difference in documented occurrence of EoL conversations in the pre-intervention cohort compared to the post-intervention cohort** (34.8%, 95% CI 28.0−42.2 vs. 33.9%, 95% CI 25.7−43.1); 2) No difference in documented DNR orders in the pre-intervention cohort compared to the post-intervention cohort (28.8%, 95% CI 22.5-36.0 vs. 27.3%. 95% CI 19.8-36.3, $P = 0.71$).
Walczak et al. (Australia, 2017) Moderate Mostly pragmatic	Parallel-group RCT / Not reported	Discussions about prognosis and end-of-life care preference and future care options	I: Patients (n = 61) received two sessions of a nurse-led communication support programme (45-min face-to-face meeting based on a question prompt list and DVD discussing ACP+15 min telephone booster session) and caregivers could join; physicians were cued to use the question prompt list and question asking during consultation C: No communication support programme for patients (n = 49) nor physicians were cued to use the question prompt list and question asking	Nurse	**Count of cues and questions for prognosis, EoL care future care options and overall for patients and their caregivers during consultations** Duration of consultation	Audio-recorded consultations	Six cancer centres / Not reported	N = 110 Advanced cancer	2-12	M: Not reported Age: Not reported	N = Not reported M: Not reported Age: Not reported	Oncologists	Not reported	1) **More overall cues and questions** ($P = 0.025$), **cues and questions about prognosis** ($P = 0.010$), **EoL care** ($P = 0.001$), and **future care options** ($P = 0.028$) **in intervention patients;** 2) **More cues and questions about prognosis in intervention family caregivers** ($P = 0.014$); 3) Unchanged consultation duration (20.6 minutes in the intervention group vs. 20.4 minutes in the control group, $P = 0.307$); 4) At one month, no difference in the overall, physical, social, emotional, or functional well-being between intervention and control.

Note. Process outcomes include occurrence, quality, timing, frequency, or duration of end-of-life conversations.
The primary outcome(s) of each study is/are in bold.
Abbreviations. ACP, Advance Care Planning; C, Control; CI, Confidence interval; d, day; DNR, Do Not Resuscitate; EoL, end of life; I, Intervention; IQR, Interquartile range; m, month; NA, Not applicable; NRS, Numeric Rating Scale; QoC, Quality of care; RCT, Randomized Controlled Trial; SE, Standard error; STAS-J, Japanese version of the Support Team Assessment Schedule.

[a] Expressed as mean (SD) if not differently specified.

*According to the Qualsyst critical appraisal criteria.

**According to the PRagmatic Explanatory Continuum Indicator Summary (PRECIS) version 2 tool.

Table 2. Process Outcomes of Interventions Aimed at Promoting End-of-Life Conversations between Professionals and Patients with Advanced Chronic or Terminal Illnesses or their Family Caregivers Assessed in the Included Studies

Author(s) (Country, year)	**Process Outcomes of Interventions Aimed at Promoting End-of-Life Conversations**									
Empty Cell	**Occurrence of End-of-Life Conversations**			**Quality of End-of-Life Conversations**				**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Empty Cell	**Occurrence of End-of-Life Conversations Documented in Medical Record**	**Occurrence of End-of-Life Conversations Documented in a Specific Module of the Electronic Medical Record**	**Patient-Reported Occurrence of End-of-Life Conversations**	**Quality of End-of-Life Conversations According to Their Content**	**Patient-Reported Quality of End-of-Life Conversations**	**Family Caregiver-Reported Quality of End-of-Life Conversations**	**Physician-Reported Quality of End-of-Life Conversations**	**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Au et al. (USA, 2012)			✓		✓					
Bickell et al. (USA, 2020)			✓		✓					
Clayton et al. (Au				✓						✓

Author(s) (Country, year)	**Process Outcomes of Interventions Aimed at Promoting End-of-Life Conversations**									
Empty Cell	**Occurrence of End-of-Life Conversations**			**Quality of End-of-Life Conversations**				**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Empty Cell	**Occurrence of End-of-Life Conversations Documented in Medical Record**	**Occurrence of End-of-Life Conversations Documented in a Specific Module of the Electronic Medical Record**	**Patient-Reported Occurrence of End-of-Life Conversations**	**Quality of End-of-Life Conversations According to Their Content**	**Patient-Reported Quality of End-of-Life Conversations**	**Family Caregiver-Reported Quality of End-of-Life Conversations**	**Physician-Reported Quality of End-of-Life Conversations**	**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
stralia, 2007)										
Connors et al. (USA, 1995)			✓							
Curtis et al. (USA, 2013)					✓	✓	✓			
Curtis et al. (USA, 2018)	✓		✓		✓					

Author(s) (Country, year)	**Process Outcomes of Interventions Aimed at Promoting End-of-Life Conversations**									
Empty Cell	**Occurrence of End-of-Life Conversations**			**Quality of End-of-Life Conversations**				**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Empty Cell	**Occurrence of End-of-Life Conversations Documented in Medical Record**	**Occurrence of End-of-Life Conversations Documented in a Specific Module of the Electronic Medical Record**	**Patient-Reported Occurrence of End-of-Life Conversations**	**Quality of End-of-Life Conversations According to Their Content**	**Patient-Reported Quality of End-of-Life Conversations**	**Family Caregiver-Reported Quality of End-of-Life Conversations**	**Physician-Reported Quality of End-of-Life Conversations**	**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Doorenbos et al. (USA, 2016)	✓				✓					
Epstein et al. (USA, 2017)				✓						
Hanson et al. (USA, 2017)	✓									
Henselmans										✓

Author(s) (Country, year)	**Process Outcomes of Interventions Aimed at Promoting End-of-Life Conversations**									
Empty Cell	**Occurrence of End-of-Life Conversations**			**Quality of End-of-Life Conversations**				**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Empty Cell	**Occurrence of End-of-Life Conversations Documented in Medical Record**	**Occurrence of End-of-Life Conversations Documented in a Specific Module of the Electronic Medical Record**	**Patient-Reported Occurrence of End-of-Life Conversations**	**Quality of End-of-Life Conversations According to Their Content**	**Patient-Reported Quality of End-of-Life Conversations**	**Family Caregiver-Reported Quality of End-of-Life Conversations**	**Physician-Reported Quality of End-of-Life Conversations**	**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
et al. (The Netherlands, 2020)										
Lakin et al. (USA, 2017)	✓	✓		✓				✓		
Lautrette et al. (France, 2007)										

Author(s) (Country, year)	**Process Outcomes of Interventions Aimed at Promoting End-of-Life Conversations**									
Empty Cell	**Occurrence of End-of-Life Conversations**			**Quality of End-of-Life Conversations**				**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Empty Cell	**Occurrence of End-of-Life Conversations Documented in Medical Record**	**Occurrence of End-of-Life Conversations Documented in a Specific Module of the Electronic Medical Record**	**Patient-Reported Occurrence of End-of-Life Conversations**	**Quality of End-of-Life Conversations According to Their Content**	**Patient-Reported Quality of End-of-Life Conversations**	**Family Caregiver-Reported Quality of End-of-Life Conversations**	**Physician-Reported Quality of End-of-Life Conversations**	**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Nakajima et al. (Japan, 2015)					✓					
Paladino et al. (USA, 2019)	✓	✓		✓				✓	✓	
Pollak et al. (USA, 2019)	✓			✓						
Reinke et al. (US	✓							✓	✓	

Author(s) (Country, year)	**Process Outcomes of Interventions Aimed at Promoting End-of-Life Conversations**									
Empty Cell	**Occurrence of End-of-Life Conversations**			**Quality of End-of-Life Conversations**				**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
Empty Cell	**Occurrence of End-of-Life Conversations Documented in Medical Record**	**Occurrence of End-of-Life Conversations Documented in a Specific Module of the Electronic Medical Record**	**Patient-Reported Occurrence of End-of-Life Conversations**	**Quality of End-of-Life Conversations According to Their Content**	**Patient-Reported Quality of End-of-Life Conversations**	**Family Caregiver-Reported Quality of End-of-Life Conversations**	**Physician-Reported Quality of End-of-Life Conversations**	**Timing of End-of-Life Conversations**	**Frequency of End-of-Life Conversations**	**Duration of End-of-Life Conversations**
A, 2017)										
Shorr et al. (USA, 2000)	✓									
Walczak et al. (Australia, 2017)				✓						✓

Table 3. Interventions Aimed at Promoting End-of-life Conversations Assessed in the Included Studies and Their Target

Epstein et al. (USA, 2017)*								✓	✓				✓	✓	✓							Multiple-session
Hanson et al. (USA, 2017)				✓	✓	✓																Multiple-session
Henselmans et al. (The Netherlands, 2020)									✓				✓	✓	✓		✓	✓				Multiple-session
Lakin et al. (USA, 2017)		✓	✓																	✓		✓	Multiple-session
Lautrette et al. (France, 2007)ǂ									✓									✓	✓				One-time
Nakajima et al. (Japan, 2015)	✓																						One-time
Paladino et al. (USA, 2019)									✓							✓	✓	✓		✓			Multiple-session
Pollak et al. (USA, 2019)			✓																		✓		Multiple-session
Reinke et al. (USA, 2017)							✓					✓											One-time
Shorr et al. (USA, 2000)		✓		✓	✓																✓		One-time
Walczak et al. (Australia, 2017)*								✓	✓	✓	✓								✓				Multiple-session

* Family caregivers could join the programme together with the patient
ǂ Only family caregivers were involved

Fig. 1. PRISMA flow-chart depicting the main stages of the systematic review process. Page MJ, McKenzie JE, Bossuyt PM. et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews.

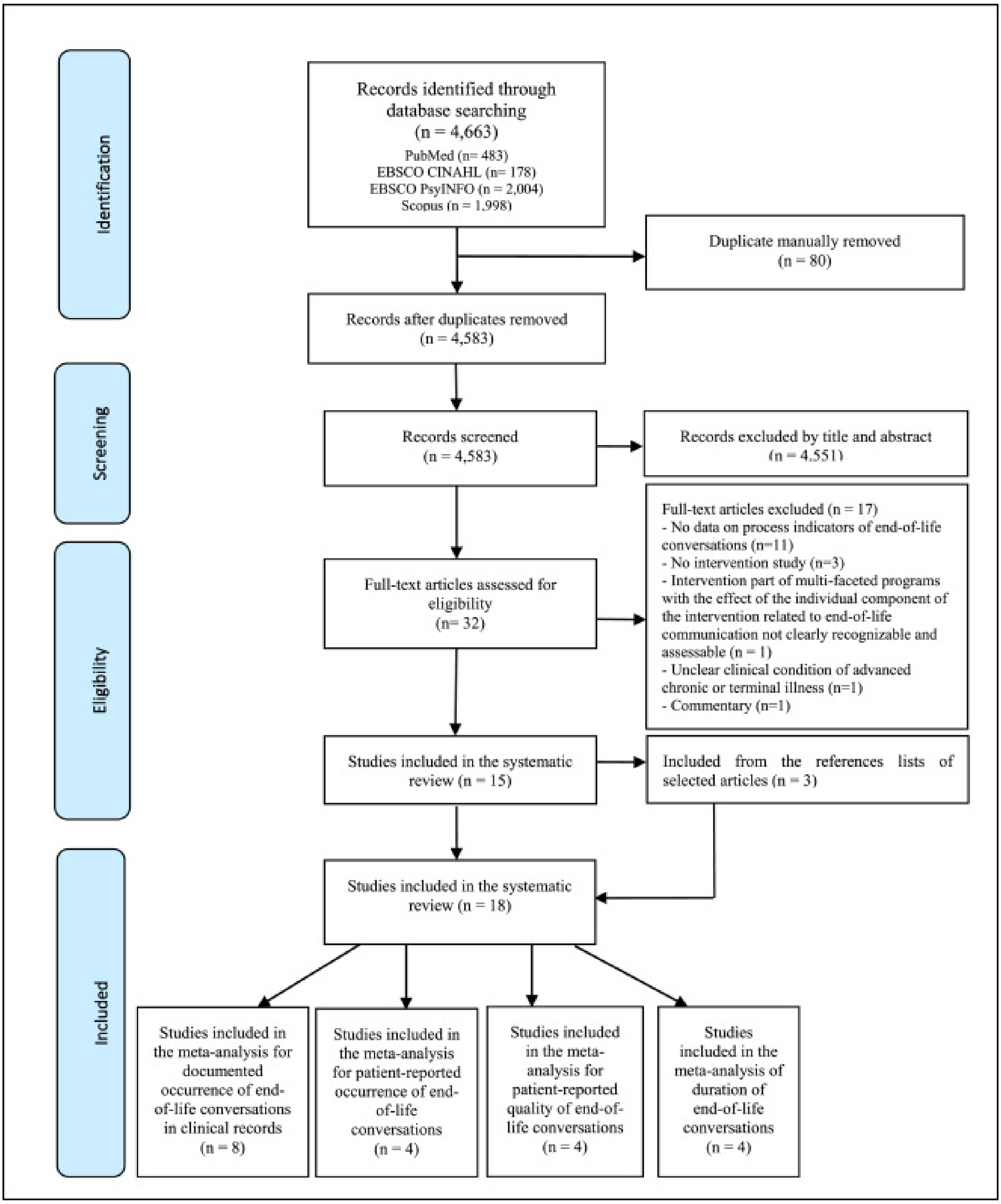

Fig. 2. Meta-analyses of interventions aimed at promoting documented occurrence in clinical records, patient-reported occurrence, patient-reported quality, and duration of end-of-life conversations. CI, Confidence interval; RR, Risk ratio; ROM, Ratio of means; SMD, Standardized mean difference.