





## REVIEW ARTICLE

# Implementation of advance care planning amid the COVID-19 crisis: A narrative review and synthesis

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Advance care planning is considered an important issue in end-of-life care for older adults. The ongoing COVID-19 pandemic has interrupted the healthcare system and end-of-life care tremendously. This review aimed to explore available articles on advance care planning amid the pandemic and analyze qualitatively. PubMed and Google Scholar were searched on February 2021 using the relevant keywords. Retrieved articles were screened applying inclusion criteria. Any article describing advance care planning during the COVID-19 era was included. A qualitative content analysis was conducted. In total, 20 articles incorporating 5542 participants from five countries were included. Among the articles, eight were primary studies and the rest were perspective papers or secondary analysis. From the qualitative content analysis six major themes emerged namely palliative care, lack of coordination among acute care, hospital palliative care, and long-term care, community-based advance care planning, real-time dissemination of scientific information on the regional pandemic situation, online system and legislation. The COVID-19 pandemic had decreased the uptake of advance care planning. Findings of the review suggested simplification of the procedure regarding advance care planning, implementation of community-based advance care planning and utilization of online resources to enhance the process. *Geriatr Gerontol Int* 2021; 21: 779–787.

**Keywords:** ACP, advance care planning, coronavirus disease, COVID-19, end-of-life care.

## Introduction

The novel Coronavirus disease 2019 (COVID-19) pandemic has led to rapid and profound changes in healthcare service delivery and society more broadly. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness.<sup>1</sup> Common ones include fever, body ache, dry cough, fatigue, chills, headache, sore throat, loss of appetite and loss of smell, while the virus is capable of causing the gravest complications: a type of pneumonia with severe respiratory symptoms in older people and those with underlying conditions such as diabetes and cardiovascular diseases.<sup>1,2</sup> The rapid spread of COVID-19 and elevated mortality rates among older populations presented significant health, economic and social challenges for governments, health services and communities.<sup>3</sup>

The current COVID-19 pandemic is also raising dilemmas worldwide concerning triage.<sup>4,5</sup> Healthcare services have been compelled to plan for worst-case scenarios in which rapid surges

in severe cases overwhelm the capacity of intensive care and other healthcare settings. The shortage of acute medical care capacity has made physicians, nurses and other allied healthcare professionals in hospitals having a considerably higher patient load and need to decide within a short time frame whom to put in or out of the intensive care system.<sup>6</sup>

In the community, long-term care or hospital settings, both the fear of infection and the need for social distancing have been limiting older people's movement and next of kin or friend visits.<sup>7,8</sup> It could lead to psychosocial distress such as social isolation and loneliness.<sup>9</sup> In particular, older people with dementia are facing unique challenges, particularly during the pandemic due to the inherent nature of the illness and the psychosocial impacts of COVID-19. They are vulnerable to a higher risk of isolation, loneliness and behavioral and psychological symptoms of dementia due to infection control measures such as physical distancing during the pandemic.<sup>10</sup> Besides, dementia compromises the decision-making capability of the individual, which poses a challenge for the implementation and uptake of advance care planning (ACP).

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The severity of the COVID-19 pandemic and the higher mortality among people with comorbidities shows that clinicians and the substitute decision-makers such as next of kin often engage in goals-of-care discussions to interpret the patients' known values. Patient's preferences under acute, often stressful conditions and the decision on which intensive care or palliative care would be in keeping with their wishes are considered. Given the medical and moral complexity of such discussions, many researchers have focused more on patient advocacy than the pre-pandemic era.<sup>11</sup>

To mitigate the possible dilemma between patient advocacy and intensive care capacity, some previous literature has suggested the implementation of ACP to the public.<sup>12</sup> ACP is a process that aims to inform and facilitate decision-making that reflects patients' preferences for future medical care at any age or stage of health.<sup>13</sup> ACP helps ensure patient treatment preferences are documented, regularly updated and respected. However, implementation of ACP has been an urgent issue to tackle since the pre-pandemic era, and the COVID-19 pandemic shows this clearly, as many older patients with chronic diseases are admitted to hospitals due to respiratory failure, and ACP discussions and documentation are often conducted in busy clinical practice settings.<sup>3,14</sup>

Although many articles dealt with factors influencing the integration of ACP in the healthcare system before the start of COVID-19,<sup>15</sup> information extracted from the literature during the COVID-19 pandemic is fragmented. The present study aims at synthesizing information from a narrative literature review to understand more broadly the challenges to implementation of ACP under the COVID-19 crisis.

## Methods

### Search strategy

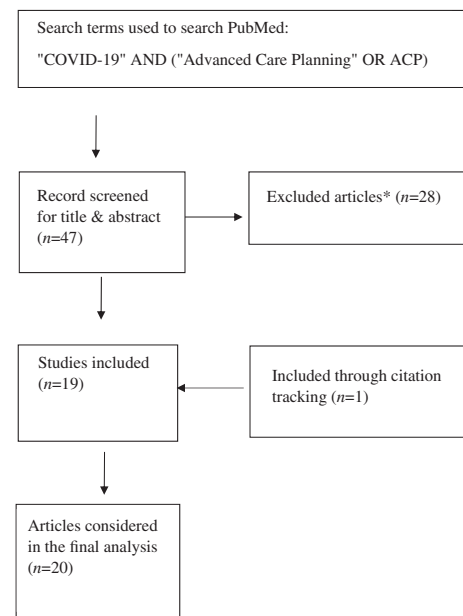
The authors used a two-faceted approach to obtain relevant material for synthesizing available scientific articles focusing on implementing ACP under the COVID-19 crisis. The authors searched Medline through PubMed, and Google Scholar in February 2021, using keywords: COVID-19, ACP and advance care planning. The keywords were combined using Boolean operators. Besides, the authors have conducted citation tracking and snowballing to get additional relevant articles.

### Eligibility criteria and selection process

The title and abstracts of the retrieved articles were screened for eligibility to include the retrieved articles. Any article demonstrating ACP in the COVID-19 context was included. Articles focusing on ACP other than in COVID-19, or articles focusing on COVID-19 but not on ACP were excluded. Only articles written in English were considered. The search was not limited to original papers, but open to any types of articles such as reviews and commentaries published in the English language in 2020 and 2021. The decision not to limit the search to original papers was based on the need to capture diverse perspectives that provide comprehensive information to understanding and address challenges for ACP during the COVID-19 pandemic. The screening and inclusion process was conducted by a review author and cross-checked to validate by the lead author. The selection process has been demonstrated in Fig. 1.

### Data abstraction and synthesis

Following qualitative synthesis of whole text data (from the introduction to conclusions) from all the relevant papers, qualitative content analysis<sup>16</sup> of the publications was undertaken to identify



**Figure 1** Article selection process. \*Causes of exclusion: not on COVID-19 = 1; not on advanced care planning = 25; not in English = 2.

key themes relevant to the topic of the present paper. Two of the authors (YH and KMSUR) read included articles and produced a coding template to identify and categorize the data into themes. All the statements mentioned in the results and discussions section were considered as representative meaning units. Each representative unit was checked and matched with similar units to group them. A new code was generated for the grouped unit. An iterative process was used throughout the analysis process until the major themes emerged. The process of creating categories and developing themes was continued until both authors reached a consensus. The findings and themes generated from the content analysis were shared with all authors who had expertise on the topic and the method. Validation of the content analysis was ensured through discussion and consensus of the author team.

## Results

### Characteristics of included articles

In total, 20 articles were included, of which eight were primary studies incorporating 5542 participants. The design of the primary studies was retrospective observational ( $n = 4$ ),<sup>17–20</sup> comparative cross-sectional ( $n = 1$ ),<sup>21</sup> design process ( $n = 2$ ),<sup>22,23</sup> quality improvement intervention ( $n = 1$ ),<sup>24</sup> case report/study ( $n = 2$ )<sup>25,26</sup> and virtual workshop ( $n = 1$ ).<sup>27</sup> The rest of the articles were perspective papers ( $n = 5$ ),<sup>3,28–31</sup> letters to the editor ( $n = 2$ ),<sup>32,33</sup> newspaper analysis ( $n = 1$ )<sup>34</sup> and guideline review ( $n = 1$ ).<sup>35</sup> The primary studies were conducted in the USA, UK, the Netherlands, Japan and Taiwan. All the primary studies included both men and women, and the mean age of the participants ranged from 62 to 78 years. Characteristics of the included studies have been described in Table 1.

Major themes evolved from the qualitative content analysis have been described here in accordance with relevance.

**Palliative care**

Although many do not have severe symptoms, older populations are more likely to develop an advanced form and be admitted to intensive care units. Because there has been no known cure so far, and consequently a significant proportion dies. Therefore, in addition to the therapeutic measures, ACP in palliative care was also required so that the patients and their families could participate in their medical care and decision-making. Anticipatory grief work is considered as a crucial component of the ACP. Some papers emphasized the significance of grieving in ACP because during the coronavirus pandemic many people have had to spend time apart from family, relatives, friends and their healthcare providers, and this can make grieving more difficult. Grief care, palliative care providers support bereavement and grief recovery by helping patients understand and process grief after the loss of a loved one is one of the essential aspects of palliative care.

“There is still a great imbalance between patients in need of palliative care services and the available specialized palliative care work force.” (Lopez *et al.*, retrospective chart review)

“Palliative interventions and the role of palliative care nurses played an integral part in addressing ethical challenges in the containment of the virus and the deleterious effects of social isolation among the elderly.” (Campos *et al.*, case study)

“The COVID-19 pandemic has disrupted the grief process for families and friends who have experienced the passing of a loved one from COVID-19.” (Reja *et al.*, letter to editor)

**Lack of coordination among acute care, hospital palliative care and long-term care**

In face-to-face interactions, mutual trust is assumed to build gradually between people and within inter-professional and inter-sector teams over time based on personal interaction and communication. However, in the absence of face-to-face contact due to the COVID-19 pandemic, it is difficult to build and maintain mutual trust in virtual collaboration. Moreover, clinical doctors and nurses in acute settings had a heavy workload and insufficient time to communicate with other sectors such as palliative care and long-term care sectors. Subsequently, due to such an overburdened condition, patients were likely to be triaged and declined by hospitals. There were also considerations around the transfer of patients, staff between acute, palliative and long-term care sectors to prevent the spread of COVID-19 infection. Lack of coordination endangered patient-provider relationships or limited the available options of end-of-life care. Amid the pandemic, the transfer of patients from hospitals to long-term care facilities is often difficult. Besides, the long-term care facilities are not always well equipped for emergency care. Similarly, ACP is strenuous to implement in emergency settings. A well-coordinated acute care service, advanced care service and long-term care service might facilitate the smooth implementation of ACP. The papers implied that under such circumstances patients faced unyielding options of end-of-life care, which is ideally provided in combination with acute and palliative care services.

“Management aligned with the patient’s goals, wishes and preferences may no longer be feasible as equity of access to life-saving technology diminishes if the health system is overwhelmed.” (Raftery *et al.*, perspective paper)

“Delegating some of the responsibility of end-of-life discussions in the transition from curative to palliative care to other health professionals who feel ready and competent may be one option.” (Raftery *et al.*, perspective paper)

“Recent changes, including strict restrictions for visitors and designated COVID units, also have made the hospital a less geriatric-friendly environment for frail nursing home residents with cognitive impairment.” (Ye *et al.*, retrospective chart review)

“Nursing homes should admit any individuals that they would normally admit to their facility, including individuals from hospitals where a case of COVID-19 was/is present.” (Gilissen *et al.*, guideline review)

**Community-based advance care planning supported by lay community people**

The surge in the admission of patients with COVID-19 to intensive care units at hospitals is complicating the provision of care to other seriously ill patients, some of whom are not receiving the medical attention they need. Overwhelmed by patients with COVID-19, hospitals struggle to treat them and other seriously ill patients and have difficulty in discussing ACP at the emergency department. There is also a lack of places with social distancing to have the ACP discussion at the hospital. Therefore, the papers of this study emphasized the community-based ACP. Community-based ACP conducted before admission could help reduce the physical and mental burden of healthcare professionals in the emergency departments. However, according to the papers, older people and their families, and healthcare professionals engaging in community care were ill-prepared for ACP practices.

“With additional training, expanding the role of dedicated social workers into becoming effective initiators of end-of-life discussions during this pandemic may also alleviate the pressure of doctors when facing the need to limit ICU admission or resuscitation.” (Raftery *et al.*, perspective paper)

“Many advantages can be seen to doing ACP before a crisis as well as revisiting these discussions over time as circumstances change.” (Rivet *et al.*, case report)

“For healthcare professionals, many remain uncomfortable discussing ACP or feel that ACP is someone else’s job.” (Block *et al.*, letter to editor)

**Table 1** Characteristics of included articles, and summary of the main findings

Author, publication year	Region; country	Study design; sample size	Study population (age, gender)	Analysis conducted	Main findings
Sinclair <i>et al.</i> , 2020 <sup>3</sup>	Global	Perspective paper	Not applicable	Not applicable	ACP should be considered as a priority and should be part of national/global COVID-19 response strategy
Gillissen <i>et al.</i> , 2020 <sup>35</sup>	Global, USA, Netherlands, Ireland, UK, Switzerland, New Zealand	Guideline review	Not applicable	Content analysis	There are limited comprehensive guidelines considering palliative care on COVID-19
Straw <i>et al.</i> , 2021 <sup>17</sup>	UK	Retrospective, observational study; 485	Mean age: 73.1 years; both men and women	Descriptive; comparison of means; age-sex adjusted and multivariable analysis	White ethnicity, comorbidity and receiving cardiovascular medications were associated with ceiling of care decisions
Reja <i>et al.</i> , 2020 <sup>32</sup>	Global	Letter to editor	Not applicable	Not applicable	Telehealth might be an important concept in end of life discussions
Raftery <i>et al.</i> , 2020 <sup>28</sup>	Global	Perspective paper	Not applicable	Not applicable	Nurse-led ACP and allied health-led ACP has been recommended
McAfee <i>et al.</i> , 2020 <sup>29</sup>	Global	Perspective paper	Not applicable	Not applicable	Recommendations to integrate death education among health professionals, teachers, undergraduate students and public
Parekh de Campos <i>et al.</i> , 2021 <sup>26</sup>	Global	Case study	Not applicable	Not applicable	Palliative care might have an role in addressing the ethical challenge of social isolation of elderly people
Nelson-Becker <i>et al.</i> , 2020 <sup>34</sup>	USA, UK	Newspaper analysis	Not applicable	Not applicable	Dying alone is stigmatized. Accompaniment or non-accompaniment should be included in ACP
Ye <i>et al.</i> , 2021 <sup>18</sup>	USA	Retrospective chart review; 963	Mean age 78; both men and women	Descriptive statistics	Proactive conversation on ACP increased the decisions on not to hospitalize or not to resuscitate
Lopez <i>et al.</i> , 2021 <sup>19</sup>	USA	Retrospective chart review; 376	Mean age 78; both men and women	Descriptive statistics; comparison of means	ACP consultations increased during the COVID-19 pandemic
Singh <i>et al.</i> , 2021 <sup>24</sup>	USA	Quality improvement intervention	Not applicable	Not applicable	Changes in management strategies positively influenced effective ACP

(Continues)

Table 1 Continued

Author, publication year	Region; country	Study design; sample size	Study population (age, gender)	Analysis conducted	Main findings
Rivet <i>et al.</i> , 2020 <sup>25</sup>	USA	Case report; 1	74 years; woman	Not applicable	Discussions on ACP guided the decision-making during COVID-19
Paladino <i>et al.</i> , 2021 <sup>22</sup>	USA	Design process	Not applicable	Not applicable	Development of a communication tool to support ACP
Lin <i>et al.</i> , 2020 <sup>20</sup>	Taiwan	Retrospective data analysis; 1126	Mean age 65.5 years; both men and women	Multivariable analysis	COVID-19 increased the outpatient ACP service
Groenewoud <i>et al.</i> , 2020 <sup>21</sup>	Netherlands, Japan	Comparative cross-sectional study; 2078	Adults; both men and women	Descriptive statistics	Japanese people preferred hospital as death place more. Dutch people preferred proactive decision of doctors
Moorman <i>et al.</i> , 2020 <sup>30</sup>	USA	Perspective paper	Not applicable	Not applicable	ACP strategy is not well oriented during acute illness
Smith <i>et al.</i> , 2020 <sup>27</sup>	USA	Virtual ACP workshop; 413	Mean age 62.4 years; both men and women	Descriptive statistics; content analysis	Virtual ACP workshops might cover a large number of target population and benefit ACP of participants
Heyland, 2020 <sup>31</sup>	Global	Perspective paper	Not applicable	Not applicable	Advance Serious Illness Preparations and Planning (ASIPP) was compared with ACP
Block <i>et al.</i> , 2020 <sup>33</sup>	USA	Letter to editor	Not applicable	Not applicable	Outpatient ACP was recommended
Tan <i>et al.</i> , 2021 <sup>23</sup>	USA	Design process; 100	Mean age 68 years; both men and women	Descriptive statistics	Nurse-led telephonic palliative care might be useful during pandemic

ACP, advanced care planning.

“Public campaign to enhance support for prognostic disclosure, open discussions on ACP by any health professional, and awareness regarding the harms of life sustaining treatments when potentially futile.” (Raftery *et al.*, perspective paper)

“Many individuals are not comfortable discussing death and dying or completing ACP, and the low rates of completion of ACP in the U.S. underscore the need for more death education of the public.” (McAfee *et al.*, perspective paper)

### **Real-time dissemination of scientific information on the regional pandemic situation**

Informed consent, a core component of ACP, allows competent patients to choose among treatments following their values, goals and priorities for their future. To avoid inappropriate decision-making, physicians must disclose enough information for the patient to make an “informed decision” about medical treatments. However, the included papers of this study implied that the COVID-19 pandemic complicated the process of informed consent during end-of-life and palliative care: the pandemic affects the provision of healthcare services. Some papers suggested the reduction in transfers to the hospital from long-term care and other community settings, while others suggested the restriction of home visiting healthcare services. Moreover, some papers suggested that up-to-date information on the real-time situation of the pandemic at the local level is important to a realistic and effective ACP as the number of patients admitted to the hospital and availability of healthcare resources change.

“Many declarants who received ACP services during the COVID-19 pandemic did so maybe because media reports opened their eyes to the importance of advance directives.” (Lin *et al.*, retrospective data analysis)

“In addition to information about the ACP process, patients and families will require up-to date information about local infection control measures (e.g. family visiting policies) to enable informed decision-making and planning.” (Sinclair *et al.*, perspective paper)

### **Online system**

Although ACP can lead to more patient-centered care, the communication around it can be challenging in acute care hospitals, where saving a life is an important priority. The COVID-19 pandemic overwhelmed the intensive care units with increased number of patients and made it difficult for hospital healthcare professionals to discuss ACP with patients, families and other team members due to lack of time and necessity of social distancing. Some papers of this study discussed the necessity of remote ACP services and integration of ACP into electronic health records.

“This simple electronic documentation is standardized across care settings, and is recognized regionally by hospitals, primary care practices and ambulance services, and facilitates timely shared decision-making amongst patients, their next-of-kin and surrogate decision makers.” (Straw *et al.*, retrospective, observational study)

“(For health practitioners) Become familiar with options for overcoming the barriers to witnessing ACD documents, such as utilizing common law directives, and in some jurisdictions through audiovisual witnessing in combination with countersigning electronic copies.” (Sinclair *et al.*, perspective paper)

“Increasing technological resources (e.g., telehealth) and expanding billing models to finance non-face-to-face goal of care and ACP encounters may also enhance the viability of inpatient palliative care teams.” (Lopez *et al.*, retrospective chart review)

### **Legislation**

Legislation to promote ACP exists in some Western countries such as the USA, Australia, Canada and the UK, although the extent and type of legislation vary. However, since the pre-COVID-19 era, some regulatory and procedural barriers were understood in the general practice context as something that limits the uptake of ACP at individual, interpersonal, provider, system and/or socioeconomic levels such as funding mechanisms and accountabilities. For example, a paper of this study suggested that the condition that two adult witnesses are required for an ACP was a barrier to disseminate ACP practices. Such barriers to the uptake of ACP worsened due to social distancing. A paper of this study suggested that low socioeconomic status households were a vulnerable population.

“The declarants can then proceed to sign the AD (advance directives) if two witnesses are available on site.” (Lin *et al.*, retrospective data analysis)

“Hospitals and states should consider temporarily pausing legal requirements for AD completion that run counter to physical distancing.” (Block *et al.*, letter to editor)

“For patients, the legal language used in most advance directives (ADs) and state-to-state variation in legal requirements, such as the need for witnesses or a notary, are all barriers to ACP, particularly in marginalized populations.” (Block *et al.*, letter to editor)

### **Discussion**

The results suggested that the COVID-19 pandemic caused restrictions of transfer, lack of time to discuss ACP and the

necessity of social distancing in healthcare settings, and had worsened the situation of ACP uptake. Under such circumstances, it was difficult for healthcare professionals to be able to listen sincerely to their values and preferences for end-of-life, make care plans that aligned with them and thus provide person-centered care. Moreover, ethical issues such as triage and resource allocation during COVID-19 prevented the normal grieving process and placed a mental burden on patients, families and healthcare professionals. The study results suggested the importance of community-based ACP, formulation of ACP online systems and legislation.

The results suggested that discussing grieving families became more important after the COVID-19 pandemic began. Before the COVID-19 pandemic, previous literature suggested that ACP might influence how caregivers adapt to loss and well-being in bereavement.<sup>22,36</sup> Discussing bereavement care in ACP can play a key role in supporting patients and families who face fear, shock and complete uncertainty, and gently prepare families for what is to come.<sup>37</sup> In general, bereavement care begins before death and is not just about the actual dying phase or time around and after death.<sup>38</sup> Partly due to limited access to hospital services and community-based healthcare services, and the necessity of social distancing measures, the COVID-19 pandemic delivered non-archetypal trajectories of social, psychological, and spiritual wellbeing and distress for family caregivers of end-of-life patients with and without COVID-19 infection.<sup>22,35</sup> Therefore, caregivers were hindered in being able to cope with grieving and loss.

The results confirmed that the COVID-19 pandemic hindered discussions surrounding ACP both inside and outside the hospital due to the overwhelming situation. To address this, research from this study highlighted the importance of ACP discussion among communities, where healthcare professionals are allowed to have sufficient time for ACP discussions with patients and families in a tranquil atmosphere. Previous studies published before the COVID-19 pandemic suggested that equipping older patients, families and community-based organizations with fundamental knowledge about ACP would promote awareness and support for person-centered care for older people living in the community and their family caregivers.<sup>39–44</sup> The results of this study also identified facilitators for implementation of community-based ACP during the COVID-19 era: updating and disseminating scientific information on the regional pandemic situation. Given the realistic decision-making, community-based ACP should include a view of how COVID-19 is affecting the capacity of local hospitals. Patient and healthcare providers engaged in community-based ACP might observe the number of infected cases, critically ill patients, and the number of hospitalization, by using available resources such as print and online media or publicly accessible hospital registry. Although, previously, data about hospital capacity that had been released was aggregated at the national or state level,<sup>45</sup> a more granular data release is needed to aggregate daily hospital reports to grasp the availabilities of acute care, palliative care and long-term care services among individual local communities across the country. The results of this study suggested that mass media plays a crucial role in facilitating community-based ACP. A huge amount of information associated with the COVID-19 outbreak was circulated by mass media throughout the globe. Previous studies showed examples of how mass media intervention during a pandemic made communities aware of personal susceptibility to and feelings of the severity of the COVID-19 and how that influenced changes on their lifestyle behavior.<sup>46</sup> A paper from this study also confirmed that mass media-led information on hospitals being overwhelmed by COVID-19 intimidated people into initiating discussions about ACP and motivated them to subscribe to their ACP forms.<sup>20</sup>

To support community-based ACP conversations, the study results suggested the importance of online ACP resources. There are existing Web-based ACP models developed in Western countries such as the USA, Ireland and Australia.<sup>47–49</sup> A previous study suggested that it is essential that important ACP information be included in the Electronic Health Record so that multiple clinicians, even from different healthcare organizations, can retrieve them, understand what is most important to patients, clarify their preferences for end-of-life care, and review all documents regularly to make sure they still accurately reflect their wishes.<sup>50</sup> In the USA, PREPARE<sup>49</sup> was developed as a new, interactive, easy-to-use, free ACP website to teach people how to identify what is important to them in life and how they want to live, how to communicate their wishes to their family and physicians in a meaningful way that can affect their medical care, and how to face complex and often scary, in-the-moment medical decisions in the context of their deeply held beliefs and values.

The results of this study suggest that ACP procedures need to be simplified so that they can reduce the risk of coronavirus infection through contact during ACP discussions and documentations. For example, social distancing measures create difficulties in getting the ACP signed face-to-face by the appropriate people and their physicians. To make matters worse, difficulties in ACP completions put vulnerable populations at risk. It has been shown for years that underserved populations, including older people living alone or in poor living condition are less likely to discuss or carry out ACP, which may result in these individuals receiving end-of-life care that is unwanted or not aligned with their values.<sup>51–54</sup>

One of the study strengths was that we conducted a qualitative content analysis of the available articles on ACP in COVID-19. This approach facilitates an in-depth exploration of the main themes discussed in these studies. To our knowledge, this is the first attempt at such an exploration and analysis. This study showed certain limitations as well. The current study is a narrative review and not a systematic one. Only two databases were searched, which might overlook some potential articles to include. The search strategy was not comprehensive, which we usually consider in systematic reviews, and only articles written in English were considered. In addition, there might be subjectivity in the inclusion process of the articles. However, to avoid subjectivity, a second reviewer cross-checked the included articles.

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## Disclosure statement

The authors declare no conflict of interest.

## Author contributions

YH and KMSUR conceptualized the research. YH and KMSUR searched, screened articles, extracted and analyzed data. YH drafted the manuscript and KMSUR provided critical input in drafting manuscript. All the authors reviewed and revised the manuscript and approved the final version.



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