

Ethical Dilemmas Surrounding the Advancement in Cancer Therapies

A Research Paper submitted to the Department of Engineering and Society

Presented to the Faculty of the School of Engineering and Applied Science
University of Virginia • Charlottesville, Virginia

In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science, School of Engineering

John Patrick Quezada

Spring 2022

On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

Advisor

Rider W. Foley, Department of Engineering and Society

Introduction

Current healthcare systems lack flexibility in their approach to patient care which limits necessary adjustments in high strain scenarios such as a pandemic. Therefore, when under strain, these healthcare systems often experience bottlenecks in their ability to deliver proper healthcare to all portions of a population. These groups that are denied quality healthcare fall under the priority population category defined by the Agency for Healthcare Research and Quality (AHRQ) (AHRQ, 2021). Included in this category are communities of color and those that are of low-socioeconomic status (SES). These healthcare disparities are driven primarily by social and economic inequities including health coverage, access to routine appointments, and pharmacy availability among others. Understanding the struggles of current healthcare systems and the resulting impacts on priority populations, this Capstone team has developed a model that can simulate approaches to healthcare resource organization and patient care during high strain scenarios. This model will be particularly useful for optimizing care for cardiovascular diseases such as strokes that require multiple interventions at the preventive, operative, and rehabilitative levels (Yan et al., 2016). In the United States, strokes also rank among the top leading causes of death meaning there is a clinical need for improvement in this area of health that this proposed model can address (Ahmad and Anderson 2021). To add, this high prevalence of stroke is having the largest impact on Black Americans, with a 45% greater likelihood of dying from stroke than their counterparts (AHA, 2020).

Cancer also ranks among the leading causes of death in the United States and will be the focus of the sociotechnical portion of this paper. There has been a notable development across history in the available treatments for cancer. Since the discovery of the first tumor in 1500 BC, the approach to treating cancer has expanded from solely surgical interventions to the use of novel

therapeutics and even mixtures of the two referred to as adjuvant therapies (Sudhakar, 2009). This expansion is in large part due to the increased knowledge of the disease from publications such as “The Hallmarks of Cancer” which introduced important concepts like oncogenic, or cancerous, mutations and the downstream effects these have on the proliferative cancer cells that become malignant (Hanahan & Weinberg, 2000, 2011). Outside of direct interventions, palliative and hospice care have become another dimension to care for chronic diseases like cancer, specifically during the end-of-life (EOL) period (Roberts, 2018). With these advances in treatment options, the assumption is that the patient’s quality of life would be improved, however, this topic requires deeper thought after considering the ethics and actors involved in medical decision making (MDM).

This will consist of first reflecting on questions that physicians and patients with cancer often face. What treatment plan will most benefit the patient? What role does the patient and their family have in the MDM process? At what time is most appropriate to engage in discussion with the patient regarding the EOL period? This will then follow with a focus on the ethical dilemmas that often arise during MDM. By definition, ethical dilemmas are scenarios that involve the need to choose between two or more courses of action that are both ethically acceptable but then mean the final decision becomes ethically unacceptable (Ong et al., 2012). These scenarios place physicians in a position of distress which can complicate their ability to properly engage in MDM. This is made more serious when physicians are frequently encountering patients in the EOL period. Given the importance of these physicians in MDM, a better understanding of what contributes to ethical dilemmas and ways to mitigate them is necessary. To provide further clarity on this subject, the sociotechnical portion of this paper will focus on analyzing ethical dilemmas surrounding the advancement in cancer therapies and identifying potential solutions.

Case Context

Within the past several decades, new therapies for treating cancer have emerged. Palliative and hospice care are some of these new therapies that specifically prioritize comfort care. This shift involves focusing more on mitigating pain during the course of treatment rather than neglecting the chronic symptoms associated with cancer. That being said, aggressive treatment options are still widely available and developing in the form of clinical trials. Rather than pursuing comfort care, patients may elect to continue seeking treatment in hopes of prolonging their life. Effective or not, the ethics behind these therapies must also be considered.

With a reported 1.55 million Medicare beneficiaries having received hospice care in 2018, and 29.6% having a cancer diagnosis, hospice is becoming a common option for patients approaching EOL (NHPCO, 2020). Patients receiving hospice care through Medicare use the Medicare hospice benefit which has certain criteria for qualification. If qualified, patients that participate in this plan receive hospice care assistance for the last 6 months of their life, although they need to give up options for further curative treatment. Terminating the option for curative treatment is concerning and one of the reasons this already sensitive conversation regarding EOL can be easily misconstrued. Instances of these criteria not correctly representing the true number of patients that needed hospice care have been previously investigated. Casarett et al. conducted a study involving three hundred cancer patients that he surveyed to determine the need for hospice care. The findings showed that 13% of these patients who were eligible with the Medicare criteria did not have a higher need relative to other pools of participants surveyed who did not meet these criteria (Casarett et al., 2009). This example stresses the importance of more applicable criteria and the high stakes involved with EOL care.

Though similar to hospice, palliative care can involve the continuation of curative treatments during the alleged EOL period. Since its first installment in 1974, it has emerged as a common option for terminal patients. As outlined by Clark in a review of palliative care, it was the idea of cancer pain management that led to the advancement of palliative care (Clark, 2007). People had started to consider the relief of pain secondary to cancer as a priority and emphasized this approach to treating patients. Since then, palliative care has become more incorporated into hospitals within the U.S. and is recognized by well-known organizations like the World Health Organization (WHO) (WHO, 2020).

Aggressive options such as chemotherapy and clinical trials have also become more common. Clinical trials are not new, however, the current advancement in medical research has made them especially relevant for the discussion of this paper. In the area of biomedical engineering, several innovations including nanomedicine and drug delivery are becoming promising for the treatment of cancer. This is because nanotherapeutics avoid secondary systemic toxicity, common with chemotherapy, by offering properties such as specificity and enhanced permeability and retention (ERP) (AZoNano, 2017). These help the drugs delivered to the site of interest stay and kill the cancer cells. The ethical concerns with nanomedicine however are in the potential for nonspecific binding in the body (Zhang et al. 2019). Like chemotherapy, this is concerning because it can lead to off-target harm to the body.

Ethical Considerations for Medical Decision Making

The sociotechnical portion of this paper seeks to provide clarity to the discussion surrounding medical ethics in the context of cancer care from the initial diagnosis to the EOL period. Second, only to heart disease, cancer remains a leading cause of death in the United States

with approximately 10 million deaths in 2020 (WHO, 2022). In response, the National Cancer Institute (NCI) and other research organizations have made commitments to improving the available funding for cancer research at institutions across the country. In fact, in 2021, the proposed NCI budget amounted to \$6.56 billion to pursue this cancer mission (NCI, 2015). Seeing that cancer prognosis presents elements of fear and uncertainty, the hope these treatments provide can make all the difference. The issues arise however when these treatments become “false hope,” misleading patients and complicating the MDM process. Unproven clinical trials often fall under this category, but so do already approved interventions. Although common cancers like melanoma with a five-year survival rate of 92.3% are more effectively treated, there are still more aggressive forms like pancreatic cancer which has a 7.3% five-year survival rate (Nuffield Trust, 2018). This cements the reality that depending on the type of cancer, the continuation of treatment may not always result in a favorable outcome. Another dimension to this problem is the ethics involved in emerging therapies. Given the complications and ethical concerns regarding the advancement in cancer therapies, the question then becomes whether this “advancement” is benefitting or hurting the care provided to cancer patients.

To understand the dynamics of MDM in the face of advancing treatment options for cancer, a review of the original “creed” for physicians is a good starting place. This creed is considered by most to be the Hippocratic Oath, an ethical framework that around 48% of all medical students across the United States are required to recite before beginning their medical training (Dossabhoy, Feng, and Desai 2018). In two comprehensive chapters, the Hippocratic Oath outlines commitments physicians must make to their patients. “Therapy and ethics” and “Value of human life” are key sections of the Hippocratic Oath that discuss the need for physicians to use their instinctual medical judgment in MDM and to avoid using any treatments that would put the

patient's life in harm's way (Antoniou et al. 2010). As are other parts of the Hippocratic Oath, these tenants are not as widely practiced in 21st-century medicine. In MDM, the opinions and concerns of the patient and the family are often weighed in with the physician's opinions forming a triad relationship. This is important to consider given the differences in motives between each person. One example is how "quality of life" is interpreted. In a 2014 pediatric study with patients undergoing cancer treatments, patients' families and physicians were surveyed on their definition of "quality of life" and the results varied drastically. It was reported that while physicians believed "quality of life" entailed minimization of pain and time in the hospital, patient parents believed that this entailed transparency in the EOL period (Valdez-Martinez, Noyes, and Bedolla 2014).

Further understanding the intricacies of MDM in cancer care requires the use of an ethical dilemma framework which will be explored in this paper. In the context of cancer, ethical dilemmas can arise soon after diagnosis and frequently throughout the course of treatment for the patient. Given the severity of cancer, this topic is already sensitive, however, the gradual rise in treatment options can make these decisions even more difficult.

Ethical dilemmas are also known to contribute to moral distress. The term moral distress was first coined by Andrew Jameton in 1984 and is defined as stress experienced by being in a situation where one is unable to act on what is morally correct (Jameton, 2017). Moral distress is often referred to in the context of nursing but is also applicable to other professions including the job of a physician in caring for patients. This is concerning not only for the mental health of the physicians themselves but also for the health of the patients being treated. If a physician is unable to make appropriate decisions regarding a patient's course of treatment on account of moral distress, this becomes problematic and requires an urgent solution for the benefit of patient care.

By investigating the ethical dilemmas that arise during MDM, moral distress and other obstacles to serving the patient can be better understood and mitigated. Above this, however, is the answer to whether the emergence of newer therapies is contributing to ethical dilemmas. Palliative care, hospice care, and clinical trials are the advancing therapies being considered and investigated through the following research methods.

Research Question and Methods

The sociotechnical portion of this paper will address the following research question: How do advances in cancer therapies give rise to ethical dilemmas during MDM? Having a better understanding of this issue has significance given the rise of new treatments becoming available for use by physicians. Two newer therapies, palliative and hospice care, are emerging in light of the prioritization of comfort care. In parallel are traditional ways of treating cancer like chemotherapy and newer approaches with nanomedicine that are undergoing clinical trials. To gain more perspective on the influence these options have had on MDM, the following research methods were conducted.

In answering this research question, a historical analysis of past and current models of MDM was conducted. This includes models that demonstrate the values of the physicians in each respective time period. These values provided insight into ethical dilemmas in the context of emerging therapies. Furthermore, the analysis of these models also included the primary means of treating cancer in that time period, whether that be surgically or with more advanced treatments. All of these treatment options were compared in relation to their influence on MDM.

To further understand the ethical dilemmas that arise during MDM, interviews with 5 physicians from surrounding Virginia hospitals were also conducted. Physicians in the palliative

and hospice care specialty were chosen given their frequent exposure to cancer patients and those in the EOL period. In each interview, physicians were asked a collection of questions (see Table 1). It must be noted that while the interviews conducted for Interviewees 2-5 used the format in Table 1, the interview for Interviewee 1 did not and was more conversational.

Table 1. Interview Questions	
Question Number	Question
Question 1	What made you decide to pursue a career in palliative care?
Question 2	How do you define “quality of life”?
Question 3	What types of ethical dilemmas do you encounter during conversations with patients receiving cancer treatment options?
Question 4	How has the advancement of cancer therapies and the number of options available contributed to these dilemmas?
Question 5	Are you aware of moral distress and has it entered your practice either personally or among other people you work with?
Question 6	Currently, what are other shortcomings of patient care for those with chronic diseases like cancer?

Results

Historical analysis of MDM models and interviews with palliative and hospice care physicians revealed several key findings. To first understand the emergence of cancer therapies, a review of these models that governed the use of cancer therapies was necessary. From the origins of medicine where medical paternalism prioritized medical intuition to the SDM of today, each model has influenced the use of therapies including those for cancer. This then asserted that it is not just the advancement of cancer therapies that are giving way to ethical dilemmas during MDM

but rather the values and priorities set by each model. It was shown that not only medical paternalism, but SDM have contributed to ethical dilemmas. Emerging options with palliative and hospice care and clinical trials both offer patient autonomy. However, this autonomy can create complications when the decisions made by the patient and their families interferes with the duty of the physician to provide quality care. Reflecting on this influence of MDM models allows for further analysis of advancing therapies and the discovery of better ways for physicians to confront ethical dilemmas and moral distress.

Models of Medical Decision Making

The approach to MDM can be summarized as a balance between medical paternalism and patient autonomy. Medical paternalism, an earlier model of MDM, was derived from the Hippocratic Oath. This model centered around the interference of the patient's autonomy for the betterment of their care. It was believed that following this approach ensured the most quality of care for patients. Medicine, however, underwent a reverse in this outlook starting in the 20th century when physicians began to consider patient autonomy (McCullough, 2011). This was evident in a review of the ethical obligations of physicians to patients outlined by professional medical organizations like the American Medical Association (AMA). Paraphrased from the 1990 *AMA Fundamental Elements of The Patient-Physician Relationship*, current standards entail that patients have the right to accept or reject a course of treatment recommended by their provider.

This shift in outlook on patient care has come with the introduction of newer models, particularly the shared decision making (SDM) model. The SDM model centers around the transparency of information with the patient during MDM. By practicing this model, it is believed that self-determination and relational autonomy, aspects of a patient's wellness, can be achieved

(Elwyn et al., 2012). This gives the patient more accountability for their course of treatment while still preserving the physician's obligation to guide them with their expertise in medicine. Evidence-based medicine (EBM) is another newer model that emphasizes the evaluation of clinical literature and research in MDM (Guyatt, 1992). As SDM attempts to alleviate ethical misconduct in MDM, EBM is similar in that it prioritizes transparency with the patient. In fact, clinicians and researchers argue that SDM and EBM actually work together and are required to ensure quality patient care (Hoffmann et al., 2014).

Model Influences on Advancing Therapies

The emergence of comfort care and clinical trials have promoted patient autonomy through SDM and EBM. Both options give the patient more autonomy to choose their course of treatment and define their quality of life. Under this premise, it is thought that these therapies may reduce the occurrence of ethical dilemmas. On the other hand, medical paternalism is the model that was presumed to have an obvious contribution to ethical dilemmas. This was based on the model's prioritization of medical intuition over patient autonomy. In fact, there are studies that have shown that these aspects of paternalism have coincided with resistance to changing the course of treatment even given a poor patient prognosis. A 2002 study showed that prognostic models that aid a physician in measuring prognosis enhance accuracy but are not being utilized (Drought & Koenig, 2002). This is problematic given the already sensitive situation patients and families are placed in during EOL scenarios. This presents an example of how paternalism can contribute to ethical dilemmas due to the lack of transparency between physician and patient.

After reconsidering SDM and its influence on palliative and comfort care, however, one must ask if there is at least some contribution here to ethical dilemmas. As a reminder, one aspect

of these therapies is the conversation with patients regarding the EOL period. A common action taken in anticipation of death is writing an advanced directive. These documents outline a patient's wishes for treatment during the EOL period given that they are no longer able to make informed decisions for themselves due to the acuity of their condition. That being said, there are arguments against the traditional advanced directive route. Clinicians argue that a patient's choices when healthy and during the EOL period are different given emotional and social biases. If a patient were to nominate a surrogate to make decisions on their behalf, it is further argued that similar biases may make this approach flawed (Sudore, 2010). This bias can lead to other ethical concerns given the weight of MDM. A 2016 study investigated the downfalls of this bias showing that non-beneficial treatments were being pursued by 33-38% of the group of patients being studied (Cardona-Morrell et al., 2016, p.). From these studies, it was realized that not only paternalism, but SDM, can contribute to ethical dilemmas.

The Impact of Moral Distress on Medical Decision Making

Underlying these ethical dilemmas is the moral distress that can be detrimental to patient care. In a collaborative study conducted in 2020, moral distress was found to be most frequent in cases where the patient was older and near the EOL period (Regenstrief Institute, 2020). It is plausible then to postulate that physicians treating patients with cancer are at a higher risk of moral distress given the severity of the disease. A literature paper published by a group of nurses and physicians identified the after-effects of moral distress on those involved in ethical dilemmas. They stated that moral residue, an extension of moral distress, can affect the healthcare worker both during patient care and in their personal life (Hamric et al., 2006). Based on this research, it is

evident that ethical dilemmas not only impact the ability of physicians to properly assess MDM but also the ability to take care of themselves both at work and at home.

Physician Perspectives on Ethical Dilemmas

Interviews with palliative and hospice care physicians offered crucial perspectives on ethical dilemmas given their personal experiences in the hospital. Although different in some respects, each interviewee had commonalities in their responses to certain questions. These responses further confirmed but also introduced previously misunderstood conceptions surrounding the advancement of cancer therapies and ethical dilemmas.

The first common ground among interviewees was that each physician prioritized patient autonomy in determining their definition of quality of life. This conversation delved into the notion that there are generally two categories of patients: those that choose the continuation of treatment in hopes of a cure and those who choose comfort care. Both of these options follow the SDM model and prioritize patient autonomy. However, in discussion with interviewees, it is evident that this may not always mitigate ethical dilemmas as previously thought. According to interviewees 2 and 4, it is not uncommon for patients to resist curative and palliative treatments even given a favorable prognosis. This presents an immediate ethical dilemma since the physician is not able to offer support despite the likelihood that it would provide real benefit to the patient.

When asked about the advancement of cancer therapies, many believed that this was a prominent contributor to the exacerbation of ethical dilemmas in MDM. In discussing the impact of this advancement, interviewee 2 stated:

“I think the advancement of science and the creation of new treatments for cancer or new cancer therapies creates this false sense of the ability of the medical community to successfully treat all forms of disease, especially cancer.”

This puts into perspective the limitations of medicine and the contradicting narrative advancing therapies present. Interviewee 3 added that many of these advancing therapies have little data to support their efficacy. This is understandable given that most are in clinical trials or only recently approved for use. Given these statements, it is valid to state that advancing cancer therapies accompanying SDM have made ethical dilemmas more common and complicated to confront.

Discussion

The STS framework of ethical dilemmas provides insight into the complications of advancing cancer therapies and MDM. This is because ethical dilemmas are a common reality that patients and physicians face. They become even more common during EOL scenarios that cancer patients are more likely to enter given the severity of the disease. Palliative and hospice care are advancements in therapies for cancer that have complicated the MDM process. Inherently, these options afford the patient comfort care, however, the poor delivery of these options is a risk for the exacerbation of ethical dilemmas. Through the review of past and current MDM models, not only paternalism, but SDM becomes more evident as contributors to ethical dilemmas. Similar evidence was provided during the interviews with palliative and hospice care physicians. The research presented explains why the advancements in cancer therapies and the models they are governed by can lead to ethical dilemmas. Without reform in the priorities our physicians and the greater healthcare system take, these ethical dilemmas are likely to continue to persist and hinder the care delivered to cancer patients.

Limitations and Caveats

Cancer is not a singular disease, meaning there are different forms that invade different parts of the body. Likewise, certain cancers are more invasive and terminal than others meaning the approach to treatment may differ from case to case. This diversity in course of treatment creates limitations to this study since the EOL scenario may not come into play for every patient with cancer. In that case, the advancement of cancer therapies will not play as much a role in exacerbating ethical concerns. The other limitation of this study is the selection bias of interviewees. All interviewees are palliative and hospice care physicians meaning they are biased toward comfort care.

Future Improvements

Future improvements to this study would include a meta-analysis of therapies available for other chronic diseases including those in the cardiovascular and pulmonary systems. Diseases in these systems such as diabetes mellitus can also lead to EOL scenarios but utilize notably different courses of treatment. Comparing the treatments available for chronic diseases would provide more insight into any disparities between diseases and the frequency of ethical dilemmas. If cancer, for instance, had a higher likelihood of physicians encountering ethical dilemmas, this would be important information to know when proposing reform to current MDM models.

Advancement of Personal Engineering Experiences

As an aspiring oncologist, this research has provided me with a different perspective on the obstacles physicians face. Prior to conducting this research, I had thought the advancement of cancer therapies was heavily positive without otherwise concerning complications. However,

reviewing MDM models that can misconstrue these therapies has made me more cognizant of a physician's duty to ensure the quality of care for patients. This was further realized in my conversation with interviewees. As we talked about the different aspects of patient care, it became clear that the healthcare system is far from perfect and requires reform. Reform that I can take initiative on, as both an oncologist and engineer, that may participate in the development and prototyping of emerging cancer therapies.

Conclusion

Ethical dilemmas are concerning realities for physicians tasked with providing quality care for cancer patients. A byproduct of ethical dilemmas, moral distress, has also been shown to not only complicate a physician's ability to provide this care but also maintain composure in their personal lives. In reviewing advancing therapies and MDM models, it is clear that these have become contributors to the ethical dilemmas faced by physicians. What was not originally understood, however, was the high influence SDM has had on the exacerbation of ethical dilemmas given its prioritization of patient autonomy. This influence was supported by interviews with palliative and hospice care physicians that described the ethical dilemmas they faced in the midst of treating patients under SDM. To better equip physicians in confronting these ethical dilemmas, a different approach to MDM is required. In defining these MDM models, advancing therapies should still be considered but there must also be improvements to the way they are incorporated. The most apparent improvement is earlier communication between physicians and patients regarding the EOL period. Taking these positive elements of SDM and redefining the way they are integrated into patient care is a way to alleviate ethical dilemmas. These changes to MDM models will also allow physicians to provide the quality of life outlined by patients from day one.

In doing so, not only will patients be better equipped to confront their cancer prognosis, but physicians will also be better equipped to encounter the ethical dilemmas they face during MDM.

Resources

- AHA. (2020, November 11). *Age-Adjusted Total Stroke Mortality Rates by Race/Ethnicity*.
Www.Heart.Org. <https://www.heart.org/en/about-us/2024-health-equity-impact-goal/age-adjusted-total-stroke-mortality-rates-by-raceethnicity>
- Ahmad, F. B., & Anderson, R. N. (2021). The Leading Causes of Death in the US for 2020. *JAMA*, 325(18), 1829–1830. <https://doi.org/10.1001/jama.2021.5469>
- AHRQ. (2021, June). *About Priority Populations | Agency for Healthcare Research and Quality*.
<https://www.ahrq.gov/priority-populations/about/index.html>
- Antoniou, S. A., Antoniou, G. A., Granderath, F. A., Mavroforou, A., Giannoukas, A. D., & Antoniou, A. I. (2010). Reflections of the Hippocratic Oath in modern medicine. *World Journal of Surgery*, 34(12), 3075–3079. <https://doi.org/10.1007/s00268-010-0604-3>
- AZoNano. (2017, October 17). *The Benefits of Nanomedicine*. AZoNano.Com.
<https://www.azonano.com/article.aspx?ArticleID=4654>
- Cardona-Morrell, M., Kim, J., Turner, R., Anstey, M., Mitchell, I., & Hillman, K. (2016). Non-beneficial treatments in hospital at the end of life: A systematic review on extent of the problem. *International Journal for Quality in Health Care*, 28(4), 456–469.
<https://doi.org/10.1093/intqhc/mzw060>
- Casarett, D. J., Fishman, J. M., Lu, H. L., O’Dwyer, P. J., Barg, F. K., Naylor, M. D., & Asch, D. A. (2009). The Terrible Choice: Re-Evaluating Hospice Eligibility Criteria for Cancer. *Journal of Clinical Oncology*, 27(6), 953–959. <https://doi.org/10.1200/JCO.2008.17.8079>
- Clark, D. (2007). From margins to centre: A review of the history of palliative care in cancer. *The Lancet. Oncology*, 8(5), 430–438. [https://doi.org/10.1016/S1470-2045\(07\)70138-9](https://doi.org/10.1016/S1470-2045(07)70138-9)

- Dossabhoy, S. S., Feng, J., & Desai, M. S. (2018). The Use and Relevance of the Hippocratic Oath in 2015-a Survey of US Medical Schools. *Journal of Anesthesia History*, 4(2), 139–146. <https://doi.org/10.1016/j.janh.2017.09.005>
- Drought, T. S., & Koenig, B. A. (2002). “Choice” in End-of-Life Decision Making: Researching Fact or Fiction? *The Gerontologist*, 42(suppl_3), 114–128. https://doi.org/10.1093/geront/42.suppl_3.114
- Elwyn, G., Frosch, D., Thomson, R., Joseph-Williams, N., Lloyd, A., Kinnersley, P., Cording, E., Tomson, D., Dodd, C., Rollnick, S., Edwards, A., & Barry, M. (2012). Shared Decision Making: A Model for Clinical Practice. *Journal of General Internal Medicine*, 27(10), 1361–1367. <https://doi.org/10.1007/s11606-012-2077-6>
- Guyatt, G. (1992). Evidence-Based Medicine: A New Approach to Teaching the Practice of Medicine. *JAMA*, 268(17), 2420. <https://doi.org/10.1001/jama.1992.03490170092032>
- Hamric, A. B., Davis, W. S., & Childress, M. D. (2006). Moral distress in health care professionals. *The Pharos of Alpha Omega Alpha-Honor Medical Society. Alpha Omega Alpha*, 69(1), 16–23.
- Hanahan, D., & Weinberg, R. A. (2000). The hallmarks of cancer. *Cell*, 100(1), 57–70. [https://doi.org/10.1016/s0092-8674\(00\)81683-9](https://doi.org/10.1016/s0092-8674(00)81683-9)
- Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of Cancer: The Next Generation. *Cell*, 144(5), 646–674. <https://doi.org/10.1016/j.cell.2011.02.013>
- Hoffmann, T. C., Montori, V. M., & Del Mar, C. (2014). The connection between evidence-based medicine and shared decision making. *JAMA*, 312(13), 1295–1296. <https://doi.org/10.1001/jama.2014.10186>

- Jameton, A. (2017). What Moral Distress in Nursing History Could Suggest about the Future of Health Care. *AMA Journal of Ethics*, 19(6), 617–628.
<https://doi.org/10.1001/journalofethics.2017.19.6.mhst1-1706>
- Mccullough, L. B. (2011). Was Bioethics Founded on Historical and Conceptual Mistakes About Medical Paternalism? *Bioethics*, 25(2), 66–74. <https://doi.org/10.1111/j.1467-8519.2010.01867.x>
- NCI. (2015, April 24). *NCI Budget and Appropriations—National Cancer Institute* (nciglobal,ncienterprise) [CgvArticle]. <https://www.cancer.gov/about-nci/budget>
- NHPCO. (2020, August 17). Hospice Facts & Figures. *NHPCO*. <https://www.nhpco.org/hospice-facts-figures/>
- Nuffield Trust. (2018, October 25). *Cancer survival rates*. The Nuffield Trust.
<https://www.nuffieldtrust.org.uk/resource/cancer-survival-rates>
- Ong, W. Y., Yee, C. M., & Lee, A. (2012). Ethical dilemmas in the care of cancer patients near the end of life. *Singapore Medical Journal*, 53(1), 11–16.
- Regenstrief Institute. (2020, February 25). *Moral distress of physicians who care for older adults: Compromising professional integrity is correlated with physician burnout and depression*. ScienceDaily.
<https://www.sciencedaily.com/releases/2020/02/200225101314.htm>
- Roberts, N. F. (2018, June 22). *The History Of Hospice: A Different Kind Of Health “Care.”* Forbes. <https://www.forbes.com/sites/nicolefisher/2018/06/22/the-history-of-hospice-a-different-kind-of-health-care/>
- Sudhakar, A. (2009). History of Cancer, Ancient and Modern Treatment Methods. *Journal of Cancer Science & Therapy*, 1(2), 1–4. <https://doi.org/10.4172/1948-5956.100000e2>

- Sudore, R. L. (2010). Redefining the “Planning” in Advance Care Planning: Preparing for End-of-Life Decision Making. *Annals of Internal Medicine*, 153(4), 256.
<https://doi.org/10.7326/0003-4819-153-4-201008170-00008>
- Valdez-Martinez, E., Noyes, J., & Bedolla, M. (2014). When to stop? Decision-making when children’s cancer treatment is no longer curative: a mixed-method systematic review. *BMC Pediatrics*, 14(1), 124. <https://doi.org/10.1186/1471-2431-14-124>
- WHO. (2020). *Palliative care*. <https://www.who.int/news-room/fact-sheets/detail/palliative-care>
- WHO. (2022). *Cancer*. <https://www.who.int/news-room/fact-sheets/detail/cancer>
- Yan, L. L., Li, C., Chen, J., Miranda, J. J., Luo, R., Bettger, J., Zhu, Y., Feigin, V., O’Donnell, M., Zhao, D., & Wu, Y. (2016). Prevention, management, and rehabilitation of stroke in low- and middle-income countries. *ENeurologicalSci*, 2, 21–30.
<https://doi.org/10.1016/j.ensci.2016.02.011>
- Zhang, Y., Li, M., Gao, X., Chen, Y., & Liu, T. (2019). Nanotechnology in cancer diagnosis: Progress, challenges and opportunities. *Journal of Hematology & Oncology*, 12(1), 137.
<https://doi.org/10.1186/s13045-019-0833-3>