

Original Research Article

Evaluation of Lung Cancer Patients Treated with Supportive Care Alone

Celikhisar Hakan, MD^{1*}, Celikhisar Aylin, MD²¹Assistant Prossessor, Department of Pulmonology, Ekol Health Group, Izmir, Turkey²Chest Diseases Specialist, Department of Pulmonology, Izmir Metropolitan Municipality Hospital, Yenisehir- Izmir-Turkey***Corresponding Author:** Celikhisar Hakan

Assistant Prossessor, Department of Pulmonology, Ekol Health Group, Izmir, Turkey

Article History

Received: 14.07.2022

Accepted: 21.08.2022

Published: 04.09.2022

Abstract: Among lung cancer patients, receiving supportive care alone is not rare. However, the clinical characteristics of these patients were not thoroughly studied. The purpose of this study is to investigate the clinical characteristics of lung cancer patients treated with supportive care alone. We retrospectively analysed the rate of lung cancer patients receiving supportive care alone in 3 separate hospitals, along with the reasons for this practice. Additionally, we investigated the histological types, palliative treatment forms, hospital consultation outcomes and places of death. A total of 611 patients were diagnosed with lung cancer from April 2016 to March 2022. 80 (13%) were treated with supportive care alone. The primary reason underlying treatment with supportive care alone in almost half of the patients was poor performance. In general, 40% of the patients received supportive care and 17% were admitted to a palliative care unit. 17% of the patients died at home and 42% in the palliative care unit. This study has revealed that 13% of the lung cancer patients with cytologic diagnoses are treated with supportive care alone, due to poor performance. 40% of these patients received supportive care at home, showing that a more accessible home care system is required for the patients and their families.

Keywords: Lung cancer, palliative treatment, supportive care.

INTRODUCTION

The incidence and mortality of cancer is increasing rapidly around the globe. According to the estimates of World Health Organization (WHO) International Agency for Research on Cancer, in 2020, 19,2 million new cases of cancer were observed globally and 9,9 million people died of cancer [1]. According to the estimates based on the available data, a 1% increase in cancer incidence and demographic changes are projected annually, and it is estimated that 26,4 million new wases of cancer and 17 million cancer-caused deaths will be observed in 2030 [2]. Lung cancer is one of the leading causes of cancer-related death globally, both in males and females [3, 4]. Despite the developments in surgical techniques and adjuvant treatment options, survival rates are still low. In spite of all recent development, the cumulative 5-year survival in lung cancer in general is still around 14% [3]. Non-small cell lung carcinoma (NSCLC) is the most common type of cancer globally and two million new cases were reported in 2019 [4]. Cases of non-small cell lung carcinoma (NSCLC) constitute 85% of all lung cancers, with the remaining 15% of the cases being of type small cell lung carcinoma (SCLC) [2]. Treatment for stage I and II NSCLC is chemotherapy or surgery plus chemotherapy, and standard treatment for stage III NSCLC is chemoradiotherapy. Also, for limited-stage SCLC, standard therapy is chemoradiotherapy. In contrary, the principal treatment for stage IV NSCLC and common SCLC is palliative chemotherapy in order to increase survival and relieve the symptoms [4]. On the other hand, both radiotherapy and chemotherapy are toxic treatments that may cause acute and permanent side effects affecting all organ systems, some of which may be fatal. Thus, supportive care is very important in these clinical conditions [5]. With the developments in supportive care and increasing use of less toxic and more active agents such as molecular-targeted medication, despite the increase in chemotherapy candidates, in practice, generally many lung cancer patients are treated with supportive care

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

CITATION: Celikhisar Hakan & Celikhisar Aylin (2022). Evaluation of Lung Cancer Patients Treated with Supportive Care Alone. *South Asian Res J Nurs Health Care*, 4(5): 72-78.

alone. However, the rate of patients and the reasons for treating these patients with supportive care alone are not thoroughly investigated. Treatment model studies are also mainly focused on chemotherapy [6]. On the other hand, treating cancer is only one dimension of all cancer treatment plans. An extensive cancer treatment cannot be provided without supportive and palliative care. Especially for oncologic patients, it is important to increase the quality of life with by preventing and mitigating pain, as well as the other physical, psycho-social and spiritual problems in terms of the type of treatment the patients receive as the healthcare services received by the patients become more complex and multi-disciplinary as they are moving towards the stages of diagnosis, treatment, supportive care and rehabilitation [5, 6]. There are few studies investigating the clinical characteristics, primary treatment location and place of death (clinic, intensive care unit, palliative care unit, home, etc.) of lung cancer patients recently diagnosed and are treated with supportive care alone. For this reason, we have conducted a retrospective research in order to assess the clinical characteristics of lung cancer patients with cytologic diagnosis, who have been treated with supportive care alone in 3 sites. In our study, we defined supportive care as the treatments provided to relieve the cancer symptoms other than surgery, radical radiotherapy and/or chemotherapy options used on primary tumours. Our aim was to present the results of the patients treated with supportive care alone.

MATERIALS AND METHODS

Patients applying to Izmir Metropolitan Municipality Eşrefpaşa Hospital, Sağlık Bilimleri University Okmeydanı Education and Research Hospital and Tire Public Hospital Pulmonology departments from April 2016 to March 2022, who have recently been diagnosed with lung cancer were enrolled in the study retrospectively. The study was approved by the local ethics committee under number 2011-KAEK-42 2019703-01 and was carried out in accordance with the Declaration of Helsinki. As the study is retrospective by nature and based on medical records, informed consent was not obtained from the subjects in person.

Patients included in the study consisted of patients cytologically diagnosed with lung cancer. As lung cancer patients not cytologically diagnosed may not actually have lung cancer, enrolment was restricted to patients diagnosed with lung cancer cytologically or histologically. Additionally, patients treated with surgical operations, radical radiotherapy and/or chemotherapy were excluded, however patients treated with palliative surgical operations or radiotherapy for distant metastatic regions were included in the study.

The clinical data in the electronic medical data of each patient were examined retrospectively. Patient characteristics including age, sex, performance and primary symptoms were evaluated retrospectively. The performance status of the patients during the treatment planning stage were evaluated. Approaches were histologic diagnosis were classified as bronchoscopy, thoracentesis, sputum and others. The reasons for receiving supportive care alone were classified as poor performance, comorbidities, patient's preference and advanced age. Although for the decision for supportive care alone had multiple reasons, each patient was classified based on the primary reason. Advanced age was defined as ≥ 80 years, except for some exceptions. For the assessment of performance, Eastern Cooperative Oncology Group (ECOG) Performance Scale was used. After consultation in our hospital, primary locations of treatment were classified as the patient's home, palliative care unit, pulmonology service or another hospital. The place of death was classified as the patient's home, general ward (service) or unknown.

Statistical Analysis

Age was reported as median and range. Other categories and patient characteristics were reported in numbers and percentages. Overall survival was defined as the duration from the date of histological diagnosis until the date of death. Survival was estimated using the Kaplan – Meier method. We utilized Cox regression analysis for calculating the non-corrected and corrected hazard ratios. The statistical significance adopted for the study was $p < 0.05$. All the analyses were performed using R software bundles (version 3.2.2; R Development Core Team, Vienna, Austria).

RESULTS

A total of 611 patients were diagnosed with lung cancer during the study period. 80 (13%) of these patients, who were treated with supportive care alone, were included in the study. 324 patients, who have undergone surgery, 175 patients receiving chemotherapy, 27 patients receiving chemoradiotherapy and 5 patients receiving radical radiotherapy were excluded. The patient characteristics are presented in Table 1. Performance status of 51% of the patients was ≥ 3 , whereas for 12% of the patients this value was 0, for 25% it was 1 and 13%, 2. Primary symptom analysis revealed that 34% of the patients had respiratory symptoms, 8% had brain involvement and 19% had bone involvement. The primary diagnosis approach was bronchoscopy (72%). Small cell lung carcinoma constituted 16% of the cases (Table 1).

Table 1: Patient Characteristics

		Number (n)	%
Age (years)	Median (range)	72 (39-90)	
Sex	Female	19	24
	Male	61	76
ECOG PS	0	10	12
	1	20	25
	2	10	13
	3	36	46
	4	4	5
Primary symptom	Lung	27	34
	Brain	6	8
	Bone	15	19
	Abdomen	11	13
	Other	21	27
Diagnostic approach	Bronchoscopy	57	72
	Thoracentesis	7	9
	Sputum cytology	4	5
	Other	12	14
Cytology	Adenocarcinoma	40	51
	Squamous cell	18	23
	Small cell	13	16
	Other	9	11
Stage	I	2	3
	II	3	3
	III	14	18
	IV	61	76
Follow-up period (months)	Median (range)	2.6 (0.0-33.1)	1

It was determined that 15% of all patients treated with supportive care alone required oxygen inhalation. 38% of these patients were prescribed with narcotic analgesics and non-steroid anti-inflammatory medication. 16% of the patients received palliative radiotherapy for bone metastases and 13% palliative radiotherapy for brain metastases. For bone and brain metastases, 2% and 3% of the patients received palliative surgery, respectively (Table 2).

Table 2: Patients receiving palliative treatment

		Number (n)	%
Palliative surgery	Bone	2	2
	Brain	3	4
	None	75	94
Palliative radiotherapy	Bone	13	16
	Brain	10	23
	None	2	3
Oxygen inhalation	Yes	12	15
	No	68	85
Pain reliever	Only NSAIDs	12	16
	Only narcotic analgesics	2	3
	NSAIDs + Narcotic analgesics	30	38

The primary reason for the practice of providing supportive care alone was poor performance in almost half of the patients, followed by patient's preference and comorbidities. The most common comorbidity was interstitial pneumonia (n=6), followed by renal failure (n=2) and haematologic diseases (n=2).

Even in cases, where aggressive treatment is recommended, some patients received supportive care alone. In patients with a performance score of 0 and 1, the most common reason for receiving supportive care alone was the preference of the patient. Among small cell lung carcinoma (SCLC) patients, similar to the primary reason for the overall patient population, the most common reason for supportive care was poor performance (Table 3).

Table 3: Reasons for providing supportive care alone

	Number (n)	%
All patients (n=80)		
Poor performance	42	52
Comorbidities	14	18
Patient's preference	15	19
Advanced age	9	11
Patients with a performance score of 0-1 (n=30)		
Comorbidities	8	27
Patient's preference	14	46
Advanced age	8	27
Small cell lung carcinoma patients (13)		
Poor performance	6	50
Comorbidities	2	19
Patient's preference	1	4
Advanced age	4	27

40% of the patients treated with supportive care alone received palliative care at home and 17% of these patients were admitted to the palliative care unit. 17% of the patients died at home and 42% at the palliative care unit (Table 4). Although SCLC patients with poor performance were regarded as chemotherapy candidates, some of these patients were unable to move due to compression of the medulla, and the others had poor performance not only due to SCLC but also to the existence of other comorbidities. Moreover, as poor performance is associated with high risk of chemotherapy-related adverse events, some patients in the high-risk group did not want to receive chemotherapy.

Table 4: Patients' primary treatment location and place of death

Primary treatment location	Number (n)	%
Home	32	40
Palliative care unit	14	17
Respiratory medicine ward	11	14
Other hospitals	23	29
Place of death		
Home	10	17
Palliative care unit	25	42
Respiratory medicine ward	16	28
Other hospitals	8	13

DISCUSSION

In our study, it was determined that only 13% of the lung cancer patients diagnosed cytologically were treated with supportive care alone. These results are consistent with the results of previous population-based studies indicating that only 9-18% of the patients were treated with supportive care alone [3, 4]. Having said that, in some studies carried out, only 25-55% of stage IV NSCLC patients were treated with chemotherapy [5, 6]. However, these studies were focused on chemotherapy and as patient populations differed among studies, these results should be interpreted carefully. Additionally, the differences between the healthcare systems of countries generally affect treatment plans. For example, in the United States of America, provision of chemotherapy is dependent on whether the patient has a private insurance policy, however, this is rarely an issue in Japan, where a universal healthcare insurance is provided. In these studies, the main reason for the provision of supportive care alone was unsurprisingly poor performance, which is consistent with the results of our study [7, 8]. Despite the recent evidence suggesting chemotherapy as a suitable treatment to NSCLC patients with a performance score of 2, these tend to cause worse clinical outcomes and higher incidence of adverse events, when compared to the patients with a performance score of 0-1 [9-11]. In general, we believe that patients with a performance score of 3-4 and some patients with a performance score of 2 should not receive chemotherapy. Thus, it is required to further develop the chemotherapy regimens for patients with poor performance.

Poor performance is not only dependent on the progression of lung cancer as comorbidities also contribute to poor performance. 50-70% of the lung cancer patients also have other diseases [12-14]. The most commonly observed comorbidities in lung care patients are chronic lung diseases, diabetes and congestive heart failure [15, 16].

In a study carried out some diseases such as congestive heart failure and chronic obstructive pulmonary disease were associated with the termination of cancer treatment, however it may be difficult to differentiate between poor

performance due to lung cancer and poor performance due to the comorbidity [17]. Therefore, in this study, the assessment of comorbidities was limited to patients with good performance scores.

When the primary treatment location of the patients was analysed, it was observed that 40% of the patients received palliative care at home and 17% of these patients were admitted to the palliative care unit. In a study carried out, it was determined that patients were more satisfied with receiving home care as compared to the institutions [18]. Many community-based survey studies have revealed that 40/-50% of the patients choose their homes as the preferred location of care and place of death [19, 20]. Our study is consistent with these results.

Median overall survival of all patients treated with supportive care alone was 3.7 months and this was consistent with the results of similar studies [3, 5, 6]. Whether home care will decrease patient survival is a source of concern. However, a retrospectively planned study has shown that the survival rate of patients receiving home care was better or at least not worse than the patients receiving palliative care at a hospital [21]. Moreover, a multi-site cohort study carried out recently has shown that cancer patients, who died at home, had similar or longer survival durations as compared to the patients dying at hospitals [22]. Our study also suggests a similar survival tendency. Although the group "Other hospitals" marked as the place of death seems like an option with better survival, this finding should be assessed carefully. In this group, 8 patients at stage I or II of the disease, who were surgery candidates, were included and it was not possible to obtain all data of each patient from these other hospitals, and these data were not sufficiently detailed. On the other hand, the group "palliative care unit" had worse survival than the group "home". The reason for this finding was not clear, however, it is possible that the conditions of these patients were so poor that they were not allowed to be discharged home or that these patients did not have any relatives, who could provide them with the care required. In terms of home care, there are various concerns including the burden on the family, not being able to respond properly to sudden changes and requirements, family practitioners' visits to the house and the expenses associated with this type of care [23, 24]. Some individuals, who preferred an acute hospital setting as the location of care tend to request the care of caregivers outside a hospital setting that is highly supported, but not experienced palliative professionals [25]. Moreover, some people believe that the quality of care at the hospital is higher than the care provided at home [26, 27]. For this reason, many patients do not prefer care at home. We believe that more accessible home care systems should be established for patients and their families. This study had some restrictions. First of all, as this is a retrospective study, it was limited to the data in the medical records, and again, for this reason we were unable to define the reasons of providing supportive care alone in a systematic manner. Secondly, all treatment plans were not developed with a council meeting consisting of the same physicians. Therefore, it is possible that different attending physicians developed different treatment plans. Thirdly, even with three sites, this was a study with a relatively small sample size, thus the generalization of the results may be limited. Overall, large observational cohort studies are required to determine the problems related to supportive care in lung cancer patients.

CONCLUSION

Our study has revealed that 13% of the lung cancer patients with cytologic diagnoses are treated with supportive care alone, mainly due to poor performance. 40% of these patients received supportive care at home, and this shows that a more accessible home care system is required for the patients and their families.

REFERENCES

1. Mattiuzzi, C., & Lippi, G. (2020). Cancer statistics: a comparison between world health organization (WHO) and global burden of disease (GBD). *European journal of public health, 30*(5), 1026-1027. doi: 10.1093/eurpub/ckz216. PMID: 31764976.
2. Boyle, P., & Levin, B. (2008). *World cancer report 2008*. IARC Press, International Agency for Research on Cancer, p. 76-81.
3. Bade, B. C., & Cruz, D. (2020). CS & Cancer, L. Epidemiology, etiology, and prevention. *Clin. Chest. Med, 41*(1-24). doi: 10.1016/j.ccm.2019.10.001. PMID: 32008623.
4. Schneider, B. J., Ismaila, N., Aerts, J., Chiles, C., Daly, M. E., Detterbeck, F. C., ... & Altorki, N. (2020). Lung cancer surveillance after definitive curative-intent therapy: ASCO guideline. *Journal of Clinical Oncology, 38*(7), 753-766. doi: 10.1200/JCO.19.02748. Epub 2019 Dec 12. PMID: 31829901.
5. De Ruyscher, D., Faivre-Finn, C., Nackaerts, K., Jordan, K., Arends, J., Douillard, J. Y., ... & Peters, S. (2020). Recommendation for supportive care in patients receiving concurrent chemotherapy and radiotherapy for lung cancer. *Annals of Oncology, 31*(1), 41-49. doi: 10.1016/j.annonc.2019.10.003. PMID: 31912794.
6. De Ruyscher, D., Faivre-Finn, C., Nackaerts, K., Jordan, K., Arends, J., Douillard, J. Y., ... & Peters, S. (2020). Recommendation for supportive care in patients receiving concurrent chemotherapy and radiotherapy for lung cancer. *Annals of Oncology, 31*(1), 41-49. doi: 10.1016/j.annonc.2019.10.003. PMID: 31912794.

7. Noonan, K., Tong, K. M., Laskin, J., Melosky, B., Sun, S., Murray, N., & Ho, C. (2014). Referral patterns in advanced non-small cell lung cancer: impact on delivery of treatment and survival in a contemporary population based cohort. *Lung Cancer*, 86(3), 344-349.
8. Nieder, C., Tollåli, T., Norum, J., Pawinski, A., & Bremnes, R. M. (2012). A population-based study of the pattern of terminal care and hospital death in patients with non-small cell lung cancer. *Anticancer research*, 32(1), 189-194.
9. Socinski, M. A., Obasaju, C., Gandara, D., Hirsch, F. R., Bonomi, P., Bunn Jr, P. A., ... & Thatcher, N. (2018). Current and emergent therapy options for advanced squamous cell lung cancer. *Journal of Thoracic Oncology*, 13(2), 165-183. doi: 10.1016/j.jtho.2017.11.111. Epub 2017 Nov 23. PMID: 29175116.
10. Davis, K. L., Goyal, R. K., Able, S. L., Brown, J., Li, L., & Kaye, J. A. (2015). Real-world treatment patterns and costs in a US Medicare population with metastatic squamous non-small cell lung cancer. *Lung cancer*, 87(2), 176-185. doi: 10.1016/j.lungcan.2014.11.002. Epub 2014 Nov 8. PMID: 25532680.
11. El-Osta, H. E., Mott, F. E., Burt, B. M., Wang, D. Y., & Sabichi, A. L. (2019). Predictors of benefits from frontline chemoimmunotherapy in stage IV non-small-cell lung cancer: a meta-analysis. *Oncoimmunology*, 8(12), e1665974. doi: 10.1080/2162402X.2019.1665974. PMID: 31741764; PMCID: PMC6844323.
12. Simone 2nd, C. B., & Jones, J. A. (2013). Palliative care for patients with locally advanced and metastatic non-small cell lung cancer. *Annals of palliative medicine*, 2(4), 178-188. doi: 10.3978/j.issn.2224-5820.2013.08.02. PMID: 25841390.
13. Nakashima, K., Akamatsu, H., Murakami, H., Niwa, T., Iwamoto, Y., Ozawa, Y., ... & Takahashi, T. (2019). Carboplatin plus nab-paclitaxel in performance status 2 patients with advanced non-small-cell lung cancer. *Anticancer Research*, 39(3), 1463-1468. doi: 10.21873/anticancer.13263. PMID: 30842183.
14. Chen, H. M., Tsai, C. M., Wu, Y. C., Lin, K. C., & Lin, C. C. (2015). Randomised controlled trial on the effectiveness of home-based walking exercise on anxiety, depression and cancer-related symptoms in patients with lung cancer. *British journal of cancer*, 112(3), 438-445. doi: 10.1038/bjc.2014.612. Epub 2014 Dec 9. PMID: 25490525; PMCID: PMC4453645.
15. Hamamoto, Y., Ibe, T., Kodama, H., Mouri, A., & Mineshita, M. (2020). Retrospective prognostic study of death at home or hospice versus at a hospital among patients with advanced non-small cell lung cancer. *American Journal of Hospice and Palliative Medicine®*, 37(2), 129-135. doi: 10.1177/1049909119865865. Epub 2019 Jul 31. PMID: 31366208.
16. Hamamoto, Y., Ibe, T., Kodama, H., Mouri, A., & Mineshita, M. (2020). Retrospective prognostic study of death at home or hospice versus at a hospital among patients with advanced non-small cell lung cancer. *American Journal of Hospice and Palliative Medicine®*, 37(2), 129-135. doi: 10.1177/1049909119865865. Epub 2019 Jul 31. PMID: 31366208.
17. Kitazawa, H., Takeda, Y., Naka, G., & Sugiyama, H. (2019). Decision-making factors for best supportive care alone and prognostic factors after best supportive care in non-small cell lung cancer patients. *Scientific reports*, 9(1), 1-9. doi: 10.1038/s41598-019-56431-w. PMID: 31882700; PMCID: PMC6934749.
18. Hanratty, B., Lowson, E., Grande, G., Payne, S., Addington-Hall, J., Valtorta N., & Seymour, J. (2014). Transitions at the end of life for older adults – patient, carer and professional perspectives: a mixed-methods study. Southampton (UK): NIHR Journals Library.
19. Shih, C. Y., Hu, W. Y., Cheng, S. Y., Yao, C. A., Chen, C. Y., Lin, Y. C., & Chiu, T. Y. (2015). Patient preferences versus family physicians' perceptions regarding the place of end-of-life care and death: A nationwide study in Taiwan. *Journal of palliative medicine*, 18(7), 625-630. doi: 10.1089/jpm.2014.0386. Epub 2015 Apr 30. PMID: 25927818; PMCID: PMC4492773.
20. Cabañero-Martínez, M. J., Nolasco, A., Melchor, I., Fernández-Alcántara, M., & Cabrero-García, J. (2019). Place of death and associated factors: a population-based study using death certificate data. *European Journal of Public Health*, 29(4), 608-615. doi: 10.1093/eurpub/cky267. PMID: 30601984.
21. Lilley, E. J., Lee, K. C., Scott, J. W., Krumrei, N. J., Haider, A. H., Salim, A., ... & Cooper, Z. (2018). The impact of inpatient palliative care on end of life care among older trauma patients who die after hospital discharge. *The journal of trauma and acute care surgery*, 85(5), 992-998. doi: 10.1097/TA.0000000000002000. PMID: 29851910; PMCID: PMC6202158.
22. Hamano, J., Yamaguchi, T., Maeda, I., Suga, A., Hisanaga, T., Ishihara, T., ... & Morita, T. (2016). Multicenter cohort study on the survival time of cancer patients dying at home or in a hospital: Does place matter?. *Cancer*, 122(9), 1453-1460. doi: 10.1002/cncr.29844. Epub 2016 Mar 28. PMID: 27018875.
23. Neergaard, M. A., Brogaard, T., Vedsted, P., & Jensen, A. B. (2018). Asking terminally ill patients about their preferences concerning place of care and death. *International journal of palliative nursing*, 24(3), 124-131. doi: 10.12968/ijpn.2018.24.3.124. PMID: 29608384.
24. Ho, C. S. (2018). The selection of death place among patients receiving hospital-based palliative care service in Taiwan. *American Journal of Hospice and Palliative Medicine®*, 35(5), 754-758. doi: 10.1177/1049909117739845. Epub 2017 Nov 15. PMID: 29141458.
25. Artico, M., D'Angelo, D., Piredda, M., Petitti, T., Lamarca, L., De Marinis, M. G., ... & Matarese, M. (2018). Pressure injury progression and factors associated with different end-points in a home palliative care setting: a

- retrospective chart review study. *Journal of pain and symptom management*, 56(1), 23-32. doi: 10.1016/j.jpainsymman.2018.03.011. Epub 2018 Mar 13. PMID: 29548891.
26. Milligan, C., Turner, M., Blake, S., Brearley, S., Seamark, D., Thomas, C., ... & Payne, S. (2016). Unpacking the impact of older adults' home death on family care-givers' experiences of home. *Health & place*, 38, 103-111. doi: 10.1016/j.healthplace.2016.01.005. Epub 2016 Feb 23. PMID: 26916987; PMCID: PMC6611724.
27. Gomes, B., Calanzani, N., Gysels, M., Hall, S., & Higginson, I. J. (2013). Heterogeneity and changes in preferences for dying at home: a systematic review. *BMC Palliat Care*, 12, 7. doi: 10.1186/1472-684X-12-7. PMID: 23414145; PMCID: PMC3623898.