A Systematic Review of Factors Influencing Older Adults' Hypothetical Treatment Decisions

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Abstract

Purpose: Cancer affects mostly older adults and although research has shown that a significant proportion of seniors do not receive treatment, little is known about the reasons why. Therefore, we conducted a systematic review of reasons why older adults accept or decline cancer treatments. Design: Systematic review of studies reporting on hypothetical cancer treatment scenarios in older patients published between inception of 10 databases and February 2013. Results: Of 17,343 abstracts reviewed, a total of 12 studies were included (sample size 21 to 511). The willingness to be treated varied by the benefits of treatment (ranging from never to always accepting the treatment), the particular side effects of treatment, and previous treatments received/previous treatment experiences (those who were treated previously were more likely to accept the same treatment). Results showed conflicting findings with regard to the impact of age, education (those with lower/higher age/education wanting more benefits before accepting), and family situation (no effect/those who were single were less likely to accept). Conclusion: Willingness among older adults to be treated was most influenced by the extent of benefits and side effects as well as prior treatment experiences. However, little is known about treatment preferences of the oldest old, those with multimorbidity, and preferences for newer agents.

Keywords

Systematic review, geriatric oncology, cancer treatment, treatment decision-making, treatment preferences, treatment refusal

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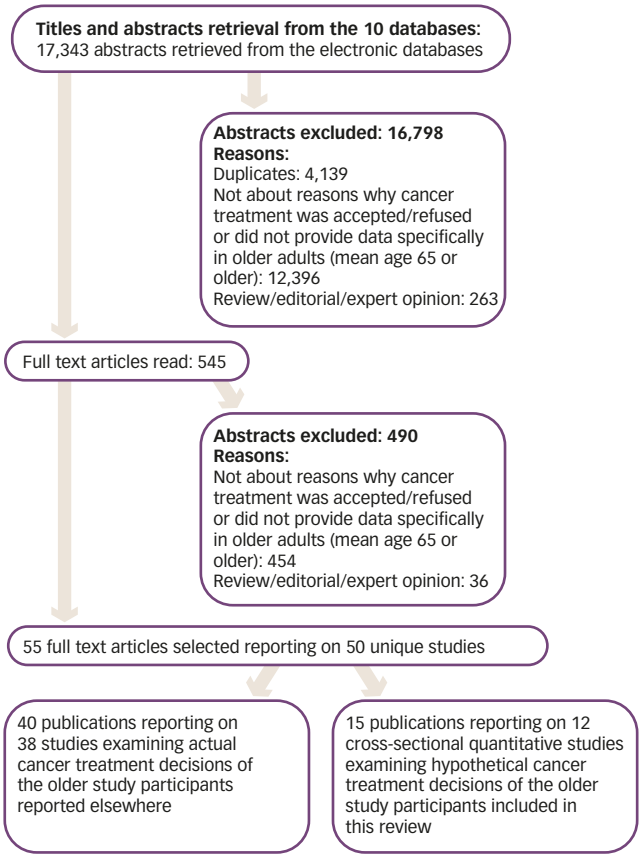
Cancer is a significant health problem in older persons.[1] It is estimated that 42 % of all incident cases and over 60 % of mortality due to cancer occur in persons aged 70 and over.[1,2] With the aging of the population there will be a considerable increase in the number of older adults diagnosed with cancer.[1,2] Treatment decisions are based on preferences, estimation of the risks and benefits, and costs. An individual makes a trade-off between

Figure 1: Flow Chart of Study Selection



the benefits and harms. However, there is less known about risks and benefits for older adults as they are underrepresented in clinical trials, particularly the more frail older adults and those with comorbidities,[3–7] which complicates treatment decision-making.

Underuse/nonreceipt of cancer treatment is commonly reported, and is more common in older adults.[8–10] Recent studies have shown underuse in 46–49 % of older patients.[11–13] Undertreatment can lead to negative outcomes, such as increased cancer recurrence rate and poorer survival. Undertreatment has been most extensively studied in older women with breast cancer.[8–10,14,15] Yood et al.[15] reported a hazard ratio of 6.25 for breast cancer mortality in older women treated for less than 1 year with hormonal therapy compared with those treated for 5 years while Verkooijen et al.[8] showed that older women who declined breast cancer surgery had a hazard ratio of breast cancer mortality of 2.1. Considering the impact of undertreatment on outcomes, it is important to understand for what reasons they would accept or decline cancer treatment. Several narrative reviews of treatment decision-making in older adults had been published[16–18] but, until now, no systematic review has been performed. One way to study treatment decision-making is by studying preferences for a certain treatment based on studying the benefits and harms of one treatment compared with other alternatives, or about an individual's preference for a certain health state compared with a perfect health state.[19]

Therefore, we conducted a systematic review with the primary objective of synthesizing all factors influencing older adults' decisions to accept or decline cancer treatment proposed by their physicians. In particular, we were interested to determine if the factors influencing older adults' decisions to accept or decline cancer treatment varied by cancer stage, cancer type, cancer treatment, and age (younger-old [65–74] versus older-old [75+]). During the conduct of our systematic review on factors influencing the treatment decisions we noticed important methodologic differences between studies studying actual treatment decisions compared with studies using hypothetical treatment decisions. Additionally, examining hypothetical treatment decision-making removes the acute stresses of making decisions while facing a diagnosis of cancer. Therefore, we decided to report the results on actual situations and hypothetical scenarios separately. In this article, we will report on the results of studies examining hypothetical treatment decisions.

Materials and Methods

Search Strategy and Selection Criteria

This review was based on a systematic, comprehensive search of 10 databases from inception to February 2013 and was conducted by an experienced health sciences librarian (ES). A study (any type of design except case studies and editorials and reviews) was eligible for inclusion if it reported on reasons why older adults with cancer (i.e. mean age study population 65 years or over or if the study mean/median age was <65 but reported results on a subgroup analysis of older adults with a mean/median age >65) accepted or declined cancer treatment and was published in English, Dutch, French, or German.

The final studies included in this review were selected in two steps based on screening of the abstract and full-text review performed independently by two reviewers (MP and BT) (see *Figure 1*). For all articles for which no mean/median age was reported, we contacted the study authors to obtain details on age. If no response was received after at least three attempts, the article was not included.

Data Abstraction

The same reviewers who performed the article-selection process conducted data abstraction independently (MP and BT). The abstracted information included study design, aim of study, location of study, sampling method, source of data, recruitment type and timeline, characteristics of study participants, details on cancer diagnosis and treatment, details on how reasons for accepting/declining cancer treatment were collected, and details of statistical analysis, source of funding, and whether or not the authors had declared any conflict of interest. No meta-analysis was conducted as the studies were too heterogeneous with regard to study population and data collected.

Quality Assessment

Both quantitative and qualitative studies were included in the review. To determine the quality of the studies included in this review the same two reviewers scored the studies using the Mixed Methods Appraisal Tool (MMAT).[20] The MMAT scoring system contains five types of mixed methods study components or primary studies, i.e. 1) qualitative; 2) quantitative randomized controlled trials; 3) quantitative nonrandomized; 4) quantitative descriptive; and 5) mixed methods with each with its own set of methodologic quality criteria based on existing published criteria. For each item the answer categories were 'yes', 'no,' or 'can't tell' followed by comments. We did not exclude

Table 1: Quality Assessment using the Mixed Methods Appraisal Tool[#]

First Author and Year Published	Type of Study	Screening Questions		Quantitative Descriptive			
		A. Are there clear research questions?	B. Do the collected data address the research question?	4.1 Is the sampling strategy relevant to address the research question?	4.2 Is the sample representative of the population under study?	4.3 Are measurements appropriate?	4.4 Is there an acceptable response rate (60 % or above)?
Blinman et al. (2010)[21]	Cross-sectional	Yes	Yes	Yes	Cannot tell, not reported	Yes	Cannot tell, not reported
Bossema (2008) et al.*[28,29]	Cross-sectional	Yes	Yes	Yes	Yes	Yes	Yes
Brundage et al. (1997)**[24,25]	Cross-sectional	Yes	Yes	Yes	Yes	Yes	No
Brundage et al. (2001)[26]	Cross-sectional	Yes	Yes	Yes	Cannot tell, not reported	Yes	No
Davidson et al. (1999)**[27]	Cross-sectional	Yes	Yes	Yes	Cannot tell, not reported	Yes	No
Extermann et al. (2003)[35]	Cross-sectional	Yes	Yes	Yes	Yes	Yes	Yes
Girones et al. (2012)[31]	Cross-sectional	Yes	Yes	Yes	Yes	Cannot tell, not reported	Yes
Harrison et al. (2008)[30]	Cross-sectional	Yes	Yes	Yes	Yes	Yes	No
Hirose et al. (2005)[32]	Cross-sectional	Yes	Yes	Yes	Yes	No	No
Hopfgarten et al. (2006)[33]	Cross-sectional	Yes	Yes	Yes	Yes	Yes	Yes
Sculpher et al. (2004)[34]	Cross-sectional	Yes	Yes	Yes	Cannot tell, not reported	Yes	Yes
Silvestri et al. (1998)[22]	Cross-sectional	Yes	Yes	Cannot tell, not reported	Cannot tell, not reported	Yes	Cannot tell, not reported
Yellen et al. (1994)[23]	Cross-sectional	Yes	Yes	Cannot tell, not reported	Cannot tell, not reported	Yes	Cannot tell, not reported

[#]None of the included studies were of another study design then quantitative descriptive, and thus these Mixed Methods Appraisal Tool criteria have been omitted from the table.
**Papers report on the same study; **Papers report on the same study.*

any study based on the quality assessment as we wanted to provide a comprehensive overview of all factors important to older adults reported in the literature.

Results

We reviewed 17,343 titles and abstracts for eligibility in the first step (see *Figure 1*) in which we selected 545 manuscripts for full text review. Of these 545, 55 manuscripts reporting on 50 unique studies were selected; 40 publications reporting on 38 unique studies examined factors influencing the older adult's decision to accept or decline treatment examined the actual cancer treatment decision taken by the study participant and reported elsewhere (manuscript submitted). There were 15 manuscripts reporting on 12 unique studies that examined hypothetical treatment decisions and these are included in this review. All manuscripts were written in English.

Quality Assessment

The quality of the studies can be seen in *Table 1*. As many studies had been published some time ago when reporting standards were less clear, for most studies there were one or more aspects of the methodology used that were not described in sufficient detail and we tried to contact all study authors for more detail. Response rates were not reported for three out of 12 studies[21–23] or were below 60 % in two out of 12 studies,[24–27] and the sampling strategy was not reported in two out of 12 studies.[21,22] The hypothetical scenarios studied were generally well described. Most scenarios were reflective of actual treatment options (i.e. were realistic) for cancer patients at the time of the study according to the study authors.[21,24,25,27–29]

Characteristics of the Included Studies

See *Table 2* for a description of included studies. Two studies were conducted in: Australia,[21,30] the US,[22,23] and Canada.[24–27] One study was conducted in:

Table 2: Description of the Included Studies

First Author and Year	Country	Study Aim	Sample Size and Response Rate	Mean/Median Age, SD (Range)
Colorectal Cancer Treatment Decisions				
Blinman et al. (2010)[21]	Australia	To determine which survival benefit would be judged as sufficient to undergo adjuvant chemo in patients with colorectal cancer	123 NR	Median age 65
Bossema (2008)*[28,29]	The Netherlands	To investigate patients' preferences for APR with a permanent stoma and LAR with sphincter preservation	122 91 %	Mean age patients in the APR group 68.6, SD 9.6; mean age LAR group 67.9, SD 10.3
Harrison (2008)[30]	Australia	To understand patients' preferences for different treatment options for rectal cancer	103 patients, 87 colorectal surgeons, 97 radiation oncologists and 80 medical oncologists. Response rates: patients 77 %, surgeons 79 %, radiation oncologists 47 %, and medical oncologists 47 %	Mean age 65 (26–88)
Lung Cancer Treatment Decisions				
Brundage (1997)**[24,25]	Canada	What improvements in survival probability would NSCLC patients like to see before accepting toxic therapy?	56 (22 lung, 34 prostate) 33 % lung, and 39 % prostate	Mean age: lung 65 years; 69 years for prostate
Brundage (2001)[26]	Canada	To examine how patients weigh both the median survival time and 1-year survival probability when considering a choice between palliative cisplatin chemo with BSC versus BSC alone for advanced NSCLC	60 32 %	Mean age 68.3, SD 10.9
Davidson (1999)**[27]	Canada	To examine actual and desired levels of involvement in treatment decisions for lung cancer and information preferences for treatment decision-making	21 33 %	Mean age 65, SD 8
Girones (2012)[31]	Spain	To examine treatment preferences and chemotherapy use in older lung cancer patients	83 100 %	Mean age 77, SD 5
Hirose (2005)[32]	Japan	To determine how patients with lung cancer weigh potential survival, chemotherapy response rate and symptom relief against the potential toxicity of different chemotherapy option	73 lung cancer patients and 120 with other respiratory illnesses 92 % for lung cancer patients	Median age lung cancer group 66 (40–80)
Silvestri (1998)[22]	US	To determine how patients with lung cancer value the trade-off between the survival benefit of chemotherapy and its toxicities	81 NR	Age <60: 38 %, age 60–70: 37 %, age >70: 25 %
Prostate Cancer Treatment Decisions				
Hopfgarten (2006)[33]	Sweden	To examine prostate cancer patients willingness to trade life for freedom from therapy-induced long-term symptoms	511 86.5 %	Mean age 71 (50–80)
Sculpher (2004)[34]	UK	To establish which attributes of conservative treatments for early prostate care are most important	129 72 %	Mean age 70 SD 6.8
Chemotherapy Decisions in Mixed Populations				
Exterman (2003)[35]	US, France	To examine the willingness to be treated with chemotherapy in older American and French cancer and noncancer patients	195 US cancer patients 78 % (n=62), noncancer patients 54 % (n=43), French cancer patients 45 % (n=36), and noncancer patients 68 % (n=54)	Mean age 77, (70–95)
Yellen (1994)[23]	US	1) To examine if age impacted the willingness to accept cancer treatment; 2) To examine if older patients are different from younger patients in trading survival for quality of life	244 (202 young (ages x–y), 42 old (ages a–b) NR	Age >65 (65–83)

**Bossema 2008–1 and Bossema 2008–2 report on the same study; **Brundage 1997, Brundage 1998 and Davidson 1999 report on the same study. APR = abdominoperineal resection; BSC = best supportive care; LAR = low anterior resection; NR = not reported; NSCLC = non-small cell lung cancer; SD = standard deviation.*

the Netherlands,[28,29] Spain,[31] Japan,[32] Sweden,[33] the UK,[34] and one in both the US and France.[35] All studies used a cross-sectional quantitative study design. Studies examined hypothetical treatment decisions for colorectal cancer,[21,28–30] lung cancer,[22,24–27,31,32] prostate cancer,[33,34] or for chemotherapy in a mixed-study population.[23,35] Sample sizes ranged between 21[27] to 511,[33] mean age ranged from 65[21,24,25,27] to 77 years.[31,35]

Factors Influencing the Treatment Decisions

Please see *Table 3* for factors influencing the treatment decisions included in each study. Below we have summarized the findings for each cancer type treatment decision separately.

Colorectal Cancer Treatment Scenarios

In the three studies examining treatment decisions for colorectal cancer, all participants had been treated for colorectal cancer. Blinman et al.[21] included 123 patients who had completed adjuvant chemotherapy for stage 2 to 3 colon cancer and asked the participants using four scenarios about their willingness to undergo treatment in exchange for increasing survival time or survival rate. They showed that 60 % of the sample would choose chemotherapy for 1 additional month of life expectancy. Half of the sample would choose chemotherapy with small benefits (1 day), while a small proportion (<5 %) would never choose chemotherapy. Participants aged 75 and older and those with higher educational levels would only accept chemotherapy for greater benefits. Bossema et al.[28,29] used the treatment trade-off and time trade-off method to examine the willingness to be treated with one of two surgical procedures, varying the risk for developing incontinence and permanent stoma as a result of the surgical procedure. All 122 participants had received surgery for stage 1–3 rectal cancer. The previously received surgery impacted the current choice: participants experiencing current incontinence were more willing to give up life years to avoid a permanent stoma (19 %) but not to avoid daily incontinence. Participants without a current stoma had a much stronger preference for the surgery that avoided a permanent stoma even if that meant incontinence monthly or daily. Similar findings were reported by Harrison et al.,[30] who reported that 65 % of 103 participants, recruited postoperatively, were willing to give up 34 % of their remaining life expectancy to avoid a stoma. Additionally, site of cancer (colon or rectal) had an effect on the choice, as did level of education, having previously received pre-operative treatment, and knowing someone who had undergone the treatment.

Lung Cancer Treatment Scenarios

Brundage et al.[24,25] studied patients who had completed chemotherapy or chemo radiation or radiation treatment for lung (n=22) or prostate (n=34) cancer and solicited preferences for high- versus low- dose radiation and preference for high-dose radiation versus chemo radiation for locally advanced non-small cell lung cancer (NSCLC). They reported that there was a wide range in survival advantage thresholds required before accepting more aggressive treatments (range 0–80 %) and a small number would always decline the aggressive treatments (4–16 %). There was no difference between the lung and prostate cancer patients and no factor (age, sex, education, or preferred role in decision-making) was associated with willingness to accept treatment. Davidson et al.,[27] reporting on the same study using the lung patients (n=21), found that essential information needed to make the treatment decision included the regimen, the side effects, the survival information, and the effect of treatment on survival probability gains. Brundage et al.[26] enrolled 60 patients treated for other cancers than lung and used the treatment trade-off method to compare when patients would choose best supportive care (BSC) (palliative radiation) versus BSC plus chemotherapy for advanced NSCLC. They showed that just over half would choose BSC plus chemotherapy for a 1-year survival advantage. Those who were older (correlation coefficient 0.30) or with no postsecondary education (correlation coefficient 0.31) had higher survival advantage thresholds before they would accept BSC plus chemotherapy. Girones et al.[31] studied 83 patients with lung cancer (all stages) who were given the choice between four treatment options: two chemotherapy regimens with survival as the main goal (a mild regimen and an intensive regimen), one chemotherapy option with no survival benefit but aiming for symptom relief, and BSC. In contrast to all other studies described above, none of the patients had yet received cancer treatment. Girones et al.[31] reported that over half of 83 patients choose treatment with survival as the treatment goal, only one-third chose BSC and only 12 % chose symptom relief. Treatment choice was associated with age, performance status, depression and dementia, and frailty. Hirose et al.[32] showed similar findings in 73 lung cancer patients who had been previously treated. They reported that the willingness of patients to accept toxicity for survival advantage varied: 19 % would choose intensive and 21 % would choose less-intensive chemotherapy if it would prolong life by 3 months; 73 % would accept intensive chemotherapy for 70 % chance of symptom relief. Although several factors were studied, only age was associated with the choice, with those aged 71–80 less likely to accept chemotherapy with smaller benefits compared with those <70 years. Similar findings, i.e. that willingness to accept more aggressive chemotherapy required larger median survival thresholds and that older patients had higher survival thresholds than younger patients, were reported by Silvestri et al.[22] in a study of 81 advanced lung cancer patients who were previously treated with chemotherapy.

Prostate Cancer Treatment Scenarios

Hopfgarten et al.[33] examined willingness to trade life expectancy (range 6 months to 5 years) to avoid long-term therapy-related side effects. They enrolled 511 prostate cancer patients of whom most had been previously treated with either surgery, radiation, and/or hormonal therapy. Most men were in the two extreme categories: they would either accept side effects for a small increase in survival probability (percentage of men ranging between 1 % and 64 %) or they would not accept the side effects no matter what the survival benefit of treatment was (percentage of men ranging from 9 % to 41 %). Age 70–80 years, being single, having a lower educational level, and having a smaller social network were associated with a lower likelihood of accepting the treatment if it induced side effects. Sculpher et al.[34] reported similar findings for 121 prostate cancer patients, some of whom had been treated with hormonal therapy. They reported that the willingness to undergo treatment was influenced by potential side effects and out-of-pocket costs (the greater the out-of-pocket costs, the less likely that patients preferred that treatment).

Mixed Cancer Population Studies with Chemotherapy Decisions as the Focus

Extermann et al.[35] included 195 mixed cancer patients from France and the US and compared willingness to be treated with chemotherapy using an intensive treatment scenario and a milder treatment scenario. Forty-five percent of French patients had received prior chemotherapy versus 86 % of American patients. Most patients in both countries would accept the

Table 3: Factors Influencing Acceptance or Decline in Hypothetical Cancer Treatment Scenarios

First Author and Year Published	Previous Treatment Received	Type of Cancer and Stage	Method of Studying Preference Used	Description Scenario	Results	Which Factors Studied to Influence Choice in Hypothetical Scenarios?	Results	Do the Scenarios Reflect Realistic Treatment Options According to Study Authors?
Decisions for Colorectal Cancer Treatment								
Blinman et al. (2010)[21]	Yes, patients have completed chemotherapy for stage II or III colon cancer	Colorectal stage II and III Adjuvant setting	Time trade-off method in 4 hypothetical scenarios	Patients were asked two types of questions about survival time and survival rate, each had two baseline prognoses (85 and 65 % for 15 and 5 years, respectively). The questions about survival time asked participants about adding extra time to their LE, questions about survival rate asked participants about adding extra percentage to the baseline survival rate	60 % of sample judged 1 month of LE beyond 5 and 15 life expectancies, and an additional 1–2 % beyond 5-year survival rates of 85 % or 65 % sufficient to choose chemo. Half the patients needed only small benefits (1 day) while 1–5 % of participants did not judge the largest survival benefits enough to make chemo worthwhile	Age, sex, employment status, children, relative who died from cancer, travel time for chemo, stage, recurrence, type of chemo, when chemo completed, having been treated in context of clinical trial, side effects of chemo experienced	Participants with tertiary education, aged 75 and younger judged larger benefits necessary to accept chemo	Yes, the situation resembled an early-stage rectal patient
Bossema (2008)*[28,29]	Yes, participants have received surgery for rectal cancer stage I–III (mean time since surgery 8 years)	Rectal Stage I–III	Treatment trade-off method and time trade-off method using two health states: good and bad health	In the treatment trade-off method, the two surgical procedures were presentation with their outcomes. The maximum risk for incontinence before switching to the other treatment was the treatment trade-off score. In the time trade-off method, one of the outcomes was permanent stoma/daily incontinence/ monthly incontinence, the other one was good health and participants were asked to make a choice between the two health states varying LE	APR patients were less willing to give up LE to be free of a permanent stoma compared with LAR patients. There was no difference between the groups to avoid daily and monthly incontinence Daily incontinence was seen as worse than monthly incontinence and a permanent stoma in both patient groups. Reasons for always choosing APR by APR patients were that the patients did not want additional surgery to remove the temporary stoma. And they thought that a there was a higher risk for a recurrence with LAR. Reasons for always choosing LAR even with daily incontinence included reluctance to have a stoma, wearing stoma bags, and/or complete removal of the anus, and 'trying' out incontinence first including tricks to reduce the impact of incontinence before switching to a permanent stoma, and the fact that a stoma could cause problems of leakage as well. Patients without the stoma had a much stronger preference score for the surgery without permanent stoma. 71 % of those with LAR always chose LAR with monthly incontinence and 32 % with daily incontinence	Current incontinence	Participants with current incontinence were more willing to give up life years to avoid a permanent stoma but not to avoid daily/monthly incontinence	Yes, LE based on population data adjusted for age and gender

Table 3: Cont.

First Author and Year Published	Previous Treatment Received	Type of Cancer and Stage	Method of Studying Preference Used	Description Scenario	Results	Which Factors Studied to Influence Choice in Hypothetical Scenarios?	Results	Do the Scenarios Reflect Realistic Treatment Options According to Study Authors?
Harrison (2008)[30]	Yes, participants were recruited postoperatively	Colorectal All stages	Prospective Measure of Preference Method, which gives 2 outcomes: willingness to trade and prospective measure of preference time trade-off	Patients were presented five treatment scenarios as well as the benefits, risks and expected long-term outcomes of each. The scenarios compared LAR with LAR plus one of four adjuvant therapies, which included postoperative radiotherapy, pre-operative radiotherapy, chemotherapy and chemoradiotherapy, and finally LAR to APR alone. Patients were then asked the proportion of their remaining LE they would trade off in order to avoid each of the treatment scenarios	The strongest preference was to avoid a stoma, with 65 % giving up a mean of 34 % of their remaining LE to avoid a stoma. The least-preferred option was LAR plus preoperative radiotherapy. 52 % was willing to give up 24 % of their LE to avoid chemoradiotherapy, followed by chemo and postoperative radiotherapy. Patients with colon cancer had stronger preferences not to have these treatments compared with rectal cancer patients and had a stronger preference not to have radiation. Lastly patients who knew somebody with a stoma were most averse against this surgical option	Cancer site, receipt of preoperative treatment, relative/friend having had stoma, relative/ friend having had radiotherapy	Those with a high level of education preferred to avoid adjuvant radiotherapy. Site of cancer was also found to be a significant determinant of preference, as more colon cancer than rectal cancer patients indicated a preference to avoid radiotherapy. Patients who had undergone preoperative treatment were less willing to trade LE to avoid chemo radiation. Finally, those who knew someone who had had an APR were more likely to indicate that they would trade LE time to avoid it	Yes, information presented to subjects was based on most current evidence available
Decisions for Lung Cancer Treatment								
Brundage (1997)**[24,25]	Yes, participants have all received treatment for NSCLC, SCLC or prostate cancer (chemotherapy or chemo radiation or radiation), finished treatments at least 2–6 weeks previously (varies by treatment received)	Lung and prostate Not reported	Treatment trade-off method	High- versus low-dose radiation therapy, and high-dose radiation therapy versus chemo radiation for locally advanced NSCLC	A wide range of thresholds for accepting aggressive treatments was reported (some would accept high-dose radiation even if benefit was 0 % to others accepting when >50 % survival benefit). If the 3-year survival advantage was 10 %, 60 % of patients would consider chemo radiation. The majority of patients would consider the more toxic therapy if it offered a certain survival benefit, but 1 % of patients would decline chemo radiation and 2 % high-dose radiation. There were no significant differences between the lung and prostate cancer patients	Age, sex, education, or preferred role in decision-making	No factor was associated with the willingness to accept more toxic therapy	Yes, the participant was asked to imagine a health state that resembled a typical patient with stage IIIb at diagnosis

Table 3: Cont.

First Author and Year Published	Previous Treatment Received	Type of Cancer and Stage	Method of Studying Preference Used	Description Scenario	Results	Which Factors Studied to Influence Choice in Hypothetical Scenarios?	Results	Do the Scenarios Reflect Realistic Treatment Options According to Study Authors?
Brundage (2001)[26]	Yes, all have been treated for cancer other than NSCLC, 15 % had chemotherapy	No active malignant disease or cancer treatment, no brain metastases	Treatment trade-off method	The patient was asked to imagine being diagnosed with advanced MSCLC Participants were described two treatment options: BSC (palliative radiotherapy to chest and hip) and BSC plus chemo (C+BSC) (radiation to hip and chemo cisplatin and vinorelbine)	57 % would choose C+BSC for 1-year survival advantage of 10 %; 36 % would choose C+BSC for median survival advantage of 1.5 months	Age, gender, education Preferred role in decision-making, previous experience with chemotherapy	Older participants tended to have higher survival advantage thresholds, as did participants who had no postsecondary education There was no relationship with gender or previous chemotherapy experience in the median survival treatment trade-off scenario these relationships were not found in the exercise with 1-year survival	Yes, the initial displays included median survivals were displayed as 4.5 (BSC) and 6 months (C+BSC). The 1-year survivals of 15 % versus 25 % Patients were informed that this represented the actual estimated survival benefits from chemo
Davidson (1999)**[27]	Yes, received low-dose RT, high-dose RT, chemo radiation surgery plus adjuvant RT for lung cancer Participants had recovered from acute side effects of treatment	Lung Not reported	Treatment trade-off method	The participant was asked to imagine being in a health stage representing the typical condition of somebody who has just been diagnosed with stageIIIB NSCLC. The participant was asked to consider and compare: low- and high-dose radiation, and then high-dose radiation to chemo radiation	Three participants were unable to do the treatment trade-off. There were patients in each group of preferred roles of decision-making (active/ collaborative or passive) that would be willing to choose the toxic treatment with little survival probability gains and patients who were unwilling to take it even if it offered 100 % probability of survival at 3 years for both treatment trade-off exercises	What information is essential for the treatment decision and what information is not important at all.	Most frequently rated essential knowledge to be: the treatment regime, side effects and survival information, and effect of treatment on disease symptoms was most important	Yes, survival information was based on clinical trial evidence
Girones (2012)[31]	No, study was conducted prior to the treatment for their lung cancer (all stages)	Lung All stages	Treatment trade-off method	Four treatment options were described to the patient, including two chemotherapy treatments for which the primary objective was survival, one option that aimed to achieve symptomatic relief, and the last was BSC. The first chemotherapy treatment was described as very intensive with severe side effects but with a greater survival advantage and the second was less intensive and better tolerated but with a modest survival advantage. The patients then had to choose their preferred therapy. The patients' actual treatment decision was made by their oncologist, independent of patient preference	The majority of patients (56.6 %) chose treatment options whose primary goal was survival. More chose the more intensive chemotherapy (38.6 %) than the less-intensive chemo treatment option (18 %). 31.3 % chose BSC while only 12 % chose symptomatic relief	PS, age, presence of depression or dementia and geriatric group	Treatment preferences were significantly related to poor health and geriatric variables, age, PS depression, dementia, and geriatric group. Elderly patients with poor PS, dementia, depression, and frailty were slightly more likely to prefer the more-intensive chemotherapy agent with a better survival advantage. Those with depression or poor PS choose option 3 more often, those without dementia choose option 1 and 2 more often, those who were independent choose option 1 more often, and frail older adults chose option 3 and 4 more often	No information provided whether the scenario reflected a realistic treatment option

Table 3: Cont.

First Author and Year Published	Previous Treatment Received	Type of Cancer and Stage	Method of Studying Preference Used	Description Scenario	Results	Which Factors Studied to Influence Choice in Hypothetical Scenarios?	Results	Do the Scenarios Reflect Realistic Treatment Options According to Study Authors?
Hirose (2005)[32]	Yes	Lung Not reported	Treatment trade-off method	Patients were presented a scenario in which they had stage IV NCSLC but were ineligible to undergo radical surgery or radiotherapy They were told that one of two types of chemotherapy, or BSC, were their only treatment options. The first form of chemotherapy was an intensive regimen whereas the second was less intensive, with fewer side effects	Patients' willingness to accept cancer treatment and its toxicity for survival advantage varied. 21 % of patients would choose to receive less intense and 19 % intensive treatment for 3 month extension of life. For a 70 % chance of symptom relief 73 % would choose intensive chemo. 41 % would accept intensive treatment for a 1 % chance of cure, 43 % would accept less intense treatment for 1 % chance of cure	Age, gender, marital status, number of dependents, and level of education	Subjects aged 40–70 were significantly more likely to accept either chemotherapy for smaller benefits compared with the 71–80 years of age patients. The other variables had no impact	No information provided whether the scenario reflected a realistic treatment option
Silvestri (1998)[22]	Yes, chemotherapy	Lung Advanced (Stage 2-4)	Adjusted Time trade-off method	Three scenarios in which each described the same patient with metastatic NSCLC with an expected survival of 4 months without treatment. In the first two scenarios (mild and severe toxicity) participates were asked the minimum survival benefit required to accept. In the last scenario patients were asked to choose between chemotherapy and supportive care when the benefit of chemotherapy was either to prolong life by 3 months or improve symptoms	The median survival threshold for accepting chemotherapy was 4.5 months for mild and 9 months for the severe toxicity scenario. When offered the choice between chemo and BSC, 22 % would choose chemo for 3 months improvement in survival and 68 % would choose chemo for symptom improvement without prolongation of life	Age	Elderly patients only accepted chemotherapy with severe toxicity at higher benefits than younger patients (accepting when survival benefit was 9.0 months versus 4.5 months in younger adults)	No information provided whether the scenario reflected a realistic treatment option
Prostate Cancer Treatment Decisions								
Hopfgarten (2006)[33]	Yes, they have received surgery, RT, and hormonal therapy	Prostate Not reported	Time trade-off method	Willingness to trade LE for avoidance of long-term-therapy-related side effects	78 % of men either accepted symptoms of fecal leakage even for the slightest probability of survival gain or would not accept no matter how long a survival gain the therapy would offer. 74 % for urinary leakage; 71 % for large tender breasts and hot flashes, 78 % for restricted diet; 73 % of men for erectile dysfunction. 41 % would not accept fecal leakage no matter what gain, 26 % no urinary leakage, 18 % no breast enlargement, 23 % no change in diet, and 9 % no impotence	Age, marital status, educational level, social network, treatment received, depressed in last 3 months	Those aged 70–80 were less likely to accept a treatment if it induced side effects compared with those 50–69, those who were single, those with lower educational level, and those who have a smaller social network	No information provided whether the scenario reflected a realistic treatment option

Table 3: Cont.

First Author and Year Published	Previous Treatment Received	Type of Cancer and Stage	Method of Studying Preference Used	Description Scenario	Results	Which Factors Studied to Influence Choice in Hypothetical Scenarios?	Results	Do the Scenarios Reflect Realistic Treatment Options According to Study Authors?
Sculpher (2004)[34]	Yes, some had or had not received anti-androgen therapy	Prostate All stages	Treatment trade-off method	Patients were provided with option a and option b and they had to choose between them while the researchers varied three attributes: 1) the ability to maintain an erection, physical energy, and libido, 2) diarrhea, hot flashes, and breast tenderness, 3) LE and out of pocket expenses	Patients were less likely to prefer a treatment if there were symptoms associated with treatment (libido, maintaining an erection, physical energy); the higher the out-of-pocket costs, the less likely the patient is to prefer that scenario; higher LE the more likely the patient is to prefer that scenario; negative values for all diarrhea, hot flashes, and breast tenderness indicate that the more severe the problem the less likely the patient is to prefer that scenario	Symptoms associated with treatment, out of pocket costs	More symptoms, less likely preferred same as for out of higher pocket costs	No information provided whether the scenario reflected a realistic treatment option
Chemotherapy Decision								
Exterman (2003)[35]	Yes, 45 % of US and 86 % of French cancer patients had received prior chemotherapy	Not reported	Treatment trade-off method	Participants were given a survey that included two scenarios: a strong chemotherapy (taxane combination-like) and a milder regime (weekly vinorelbine-like) Side effects were described in the scenarios. Patients were asked their willingness to accept under varying chances of cure, life prolongation, or symptom relief. They could also refuse the treatment	For each treatment the levels of willingness were similar for cancer patients from both countries. 70.5 % of US and 77.8 % of French patients would accept strong chemo and 88.5 % of US and 100 % of French cancer patients would accept the mild chemo	Functional status, PS, depression, self-rated health, marital status, education, presence of a caregiver, tumor type, and previous treatment	Among cancer patients, those with better self-rated health were less likely to reject the mild regimen	No information provided whether the scenario reflected a realistic treatment option
Yellen (1994)[23]	10/39 of the older patients have been treated and 182/202 of the younger patients have	Mixed: breast, GI, lung, lymphoma, and others All stages	Switch point vignettes	Patients were read a vignette of a patient of the same sex and same cancer. Two vignettes described a patient with early stage and two with advanced metastatic disease	The effect of age on the point at which patients switched their preference was significant for both the advanced-disease (p=0.036) and early-stage disease (p=0.050) vignettes; in early stage, point at which switch occurred in younger adults was when survival advantage dropped to 77.4 %, contrasting the mean switch percentile of 69.9 % for older adults. This effect was replicated in the advanced stage vignette point at which younger adults switched to the more toxic treatment was 67.9 % versus 61.9 % for older; younger adults are more likely to trade QOL for an increased survival advantage than their older counterparts, irrespective of stage of disease	Sex, disease stage, diagnostic category, race, PS, setting, previous chemo, past treatment difficulty	Younger adults (<65) are more likely to trade QOL for an increased survival advantage than their older (>65) counterparts, irrespective of stage of disease, choices about treatment preference appeared related to past experience with chemotherapy, age did not interact with past experience of past treatment history to influence aggressiveness of preferences; however, those who experienced difficulty with previous treatments were less aggressive	No information provided whether the scenario reflected a realistic treatment option

**Bossema 2008–1 and Bossema 2008–2 report on the same study; **Brundage 1997, Brundage 1998, and Davidson 1999 report on the same study. APR = abdominoperineal resection; BSC = best supportive care; GI = gastrointestinal; LAR = low anterior resection; LE = life expectancy; NA = not available; NR = not reported; NSCLC = non-small cell lung cancer; PS = performance status; QOL = quality of life.*

Table 4: Summary of Factors Significantly Influencing the Decision to Accept the Treatment Included in the Hypothetical Scenario

First Author and Year Published	Decision Studied	Age	Sex	Education	Marital Status/Living Circumstances	Socio-economic Circumstances	Previous Treatment Experience	Health and Therapy-related Factors	Psychosocial
Colorectal Cancer Decisions									
Blinman et al.(2010)[21]b	What survival benefits would be worthwhile to accept adjuvant chemotherapy	Age less than 75 needed larger benefits to accept treatment	NS	Those with graduate education needed larger benefits to accept treatment	NS	NS		NS	
Bossema [28,29]*a	Willingness to accept APR or LAR against varying levels of fecal incontinence or stoma						Previous experience of living with stoma or incontinence influenced the chance of choosing APR/LAR	The chance of incontinence impacted the choice	
Harrison (2008)[30]b	Willingness to trade survival against surgical and adjuvant treatment options			Highly educated persons were more willing to trade survival to avoid RT			Patients with pre-operative treatment were less likely to trade survival to avoid RT Patients with a friend/relative who had an APR with stoma were more likely not to choose this option	Patients with colon cancer were more willing to trade survival to avoid RT	
Lung Cancer Decisions									
Brundage (1997)** [24,25,27]a	Willingness to trade survival when making a choice between low- and high-dose RT and between high-dose RT and chemotherapy	NS	NS	NS					
Brundage (2001)[26]a	Willingness to trade survival when making a choice between chemotherapy plus BSC versus BSC alone	Older patients required larger survival benefits to accept treatment	NS	Those with no lower education required larger benefits			NS		
Girones (2012)[31]a	To examine choice for 4 lung cancer treatments and patient preferences and patient characteristics	Older patients were more likely to choose aggressive treatments						Poor PS or frailty more likely to choose aggressive treatment	Patients with depression/dementia more likely to choose aggressive treatment
Hirose (2005)[32]a	Willingness to trade survival, chemotherapy response rate against toxicity of different chemotherapy options	Those >70 years of age were less likely to accept mild and intense chemo for small benefits	NS	NS	NS				

Table 4: Cont.

First Author and Year Published	Decision Studied	Age	Sex	Education	Marital Status/Living Circumstances	Socio-economic Circumstances	Previous Treatment Experience	Health and Therapy-related Factors	Psychosocial
Silvestri (1998)[22]a	Willingness to trade survival when making a choice between chemotherapy with different toxicity levels and between chemotherapy and BS	Older patients required larger survival benefits to accept treatment	NS				Those who had lower quality of life during their treatment required larger benefits to accept treatment		
Chemotherapy Decision for Mixed Population									
Exterman (2003)[35]b	Willingness to trade survival, chance of cure and symptom relief against toxicity of different chemotherapy options	NS	NS			French patients were less likely to accept treatment than US patients		Patients with better self-rated health are less likely to reject mild chemotherapy	
Yellen (1994)[23]a	Willingness to trade survival against quality of life and toxicity of different chemotherapy options	Older patients were less likely to trade quality of life for benefits in survival	NS				Patients who previously experienced chemotherapy-related problems chose less-aggressive treatment	NS	
Prostate Cancer Decisions									
Hopfgarten (2006)[33]a	Willingness to trade survival for freedom of side effects	Those aged 70–80 were less likely to accept treatment		Those with a low educational level were less likely to accept treatment	Those who were single were less likely to accept treatment, those with few friends were less likely to accept treatment		NS	Specific side effects influence choice	NS
Sculpher (2004)[34]a	Willingness to trade survival against different side effects of treatment and out of pocket expenses	Older men were less influenced by the ability to maintain an erection when choosing a treatment				The higher the costs the less likely the choice for that treatment		The more severe the side effects the less likely patients are to accept that treatment	

**Bossema 2008–1 and Bossema 2008–2 report on the same study; **Brundage 1997, Brundage 1998, and Davidson 1999 report on the same study. aVariables tested in univariable analysis only; bVariables tested in multivariable model. For each study, we identified all variables that were examined by study authors. APR = abdominoperineal resection; BSC = best supportive care, LAR = low anterior resection; NS = not significant relationship; RT = radiation therapy; PS = performance status.*

mild regimen and 70–77 % would accept the intensive regimen. Although several potential influential factors were studied, only self-rated health had an impact on the mild chemotherapy decision (those in better self-rated health were less likely to reject the mild chemotherapy regimen). Yellen et al.[23] reported that 42 patients >65 years were less likely to trade quality of life for survival than those <65, and that the choice of treatment was related to patient experience with chemotherapy (e.g. those who had experienced problems with the previous treatment were less aggressive). A quarter of patients had been treated prior to the study.

Summary Factors Influencing the Decision to Accept the Treatment

Table 4 summarizes all factors influencing the decision to accept treatment. With regard to our research question, if older adults' decisions varied by cancer stage, cancer type, cancer treatment, and age, there are mixed results. There are conflicting findings for the influence of age, education, marital status, and previous treatment experience; in some studies, these factors led to increased likelihood of treatment acceptance whereas in other studies it decreased the likelihood of accepting treatment. Only one

Table 5: Minimum Increase in Survival Rate and Life Expectancy that Participants Considered Worthwhile

First Author and Year Published	Minimum Increase in Survival Rate			Minimum Increase in Life Expectancy				
	5-year Survival Rate Without Treatment	Median Desired Increase (%)	Range (%)	Participants Unwilling to Accept Treatment (%)	Life Expectancy Without Treatment (Years)	Median Desired Increase	Range	Participants Unwilling to Accept Treatment (%)
Decisions for Colorectal Cancer								
Blinman et al.(2010)[21]b	65 %	0.1	0.1–35	0	5	1 month	1 day-15 years	0
	85 %	0.1	0.1–35	0	15	1 month	1 day-15 years	5
Other Outcomes Studied								
Decisions for Lung Cancer								
	Outcome 1 Studied	Median Desired Increase (%)	Range (%)	Participants Unwilling to Accept Treatment (%)	Outcome 2 Studied	Median Desired Increase	Range	Participants Unwilling to Accept Treatment (%)
Brundage (1997)*[24,25,27]a	Survival advantage threshold 6-month endpoint	10	3–25	17				
	Survival advantage threshold 1-year endpoint	15	10–30	9				
	Survival advantage threshold 3-year endpoint	10	2–30	6				
Brundage (2001)[26]a	1-year survival advantage threshold	10	43–70	NR	Median survival benefit threshold	1.5 month	NR	NR
Hirose (2005)[32]a	Chance of cure to accept intensive treatment	10	NR	NR	Willingness to accept intensive chemo threshold	10 months	0–60	<5 %
	Chance of cure to accept less-intensive treatment	7	NR	NR	Willingness to accept less-intensive chemo threshold	20 months	0–60	<5 %
Silvestri (1998)[22]a					Willingness to accepted chemotherapy with mild toxicity threshold	4.5 months	NR	NR
					Willingness to accept chemotherapy with severe toxicity threshold	9.0 months	NR	NR

**Brundage 1997, Brundage 1998, and Davidson 1999 report on the same study. aVariables tested in univariable analysis only; bVariables tested in multivariable model. NR = not significant relationship.*

study by Brundage et al.[24,25] directly compared if the treatment choice varied by cancer type and showed no difference. With regard to differences in preference due to cancer stage, this was not studied. With regard to comparing preferences for the different cancer treatment modalities, most studies examined the preference of older adults for one of two/three alternative treatments and the type of treatment and potential side effects/toxicity did influence the choice. The findings across all included studies show similar factors to be important, but, as mentioned above, with conflicting findings about the direction of the association. *Table 5* shows the results of the willingness to trade survival against different treatment toxicities showing varying willingness to trade survival are described.

Discussion

To our knowledge, this is the first systematic review focusing on reasons why older adults with cancer accept or decline cancer treatments focusing on studies using hypothetical treatment scenarios. The results showed that the willingness to be treated varied by the benefits of treatment, the particular side effects and previous treatments received/previous treatment experiences. The results also showed conflicting findings in terms of the impact of social status, education, and family situation. None of the reported studies examined the impact of comorbid conditions on treatment preferences but this is be hypothesized to impact older adults' preferences; persons who have been diagnosed with other life-threatening conditions prior to cancer may be less shocked and more experienced in making treatment decisions. In addition, comorbid conditions do impact cancer specialists' treatment recommendations.[36–41] Only Girones et al.[31,42,43] reported the level of frailty in the older participants that is common in older adults. Frailty can impact both treatment tolerability and efficacy[44–48] as well as the treatment delivery, as not all older frail patients will be able to attend a clinic or hospital independently to receive treatment, and thus the general level of frailty of older study participants should be described. As the older population is the most heterogeneous in terms of health and functional status, it is important to have a good assessment of the health and well-being (i.e. geriatric assessment) to inform treatment choices as well as to be able to communicate the potential risks and benefits of treatment, which is crucial for patients' willingness to be treated or not.[49] In addition, this information will also help the oncologist with developing treatment recommendations. A recent qualitative study of medical oncologists showed considerable variation in treatment recommendations in patients with advanced cancer, and factors such as the physician's

perception of patient age and life circumstances influenced the treatment recommendation.[50] A geriatric assessment will make the decision based on more objective clinical data and less based on clinical judgments. And with a better estimation of risks and benefits, patients can make more informed choices. A recent systematic review of patients' awareness of disease status did show that this awareness impacted treatment preferences and quality of life.[51] With the aging of the population, many older patients have more than one chronic condition for which they face treatment decisions. These treatment recommendations may even be conflicting.[52–55] Therefore, the discussion about treatment goals is crucial for older adults to make informed treatment decisions. However, a recent report of the Institute of Medicine Delivering High-Quality Cancer Care[56] reported that patients are not always well informed and recommended that patients to be more informed and engaged with the treatment decision-making process as well as more research on older cancer patients and patients with multimorbidities to improve patient centeredness and engagement.

This review showed important gaps in current knowledge. Although we focused on studies with older adults, there were only four studies with a mean age in the seventies (two studies low seventies[33,34] and two studies mean of 77 years[31,35]), and thus little is known about the treatment preferences of the oldest old patients. Similarly, while most studies have focused on lung, colorectal, and prostate cancer, little is known about older adults facing other cancer diagnoses and/or treatments. Furthermore, several of the studies were conducted more than a decade ago. Since then new treatments have been introduced in clinical practice with many of them being oral agents with different risks, benefits, and mode of administration, so it is important to study willingness to be treated with newer, more 'elder-friendly' regimens. Similarly, it is important to study the impact of comorbidities, health literacy, and family support on willingness to be treated and also learn more about the oldest old patients. In addition, it is important to understand how we can support older adults facing cancer treatment decisions who have multimorbidity, as this has not been studied. Lastly, there is little known about the role of the family caregiver in the treatment decision-making process for older adults, while many older adults with cancer are dependent on caregivers for support (e.g. cognitive, emotional, practical, such as transportation, and management of side effects) and thus their role on treatment decision-making should be included in future studies.

This systematic review has several strengths. First, a systematic approach to appraise the literature was used with two independent reviewers reviewing the abstracts and manuscripts and abstracting data. Second, our search was very inclusive as we conducted the search in 10 electronic databases and articles published in four languages. Third, we were comprehensive, no study was excluded based on the quality assessment score and studies using both qualitative and quantitative studies were eligible; however, only studies using a quantitative design were found. However, many studies had a response rate below 60 % or it was not reported, thus there may be selection bias that influences the results of these studies. Furthermore, this review also has limitations. As in any review, the findings are limited by the methodologic quality of the included studies and as many studies were reported a while ago when reporting standards were less clear, there was missing information on response rates and sampling strategies used. Even though we tried to contact all study authors using multiple attempts and using the internet to find current contact information, we were not able to contact all authors and obtain all missing methodological details of the included studies. Last, the studies were too heterogeneous to conduct a meta-analysis.

In conclusion, treatment preferences are influenced by age, social support, potential benefits and risks, and previous treatment experiences. More research is needed to study treatment preferences taking into account multimorbidity, including the oldest old populations, and examining willingness to be treated with newer treatments such as oral agents and/or targeted agents. ■

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