

# Defining Undertreatment and Overtreatment in Older Adults With Cancer: A Scoping Literature Review

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**PURPOSE** The terms undertreatment and overtreatment are often used to describe inappropriate management of older adults with cancer. We conducted a comprehensive scoping review of the literature to clarify the meanings behind the use of the terms.

**METHODS** We searched PubMed (National Center for Biotechnology Information), Embase (Elsevier), and CINAHL (EBSCO) for titles and abstracts that included the terms undertreatment or overtreatment with regard to older adults with cancer. We included all types of articles, cancer types, and treatments. Definitions of undertreatment and overtreatment were extracted, and categories underlying these definitions were derived through qualitative analysis. Within a random subset of articles, C.D. and K.P.L. independently performed this analysis to determine final categories and then independently assigned these categories to assess inter-rater reliability.

**RESULTS** Articles using the terms undertreatment ( $n = 236$ ), overtreatment ( $n = 71$ ), or both ( $n = 51$ ) met criteria for inclusion in our review ( $n = 256$ ). Only 14 articles (5.5%) explicitly provided formal definitions; for the remaining, we inferred the implicit definitions from the terms' surrounding context. There was substantial agreement ( $\kappa = 0.81$ ) between C.D. and K.P.L. in independently assigning categories of definitions within a random subset of 50 articles. Undertreatment most commonly implied less than recommended therapy (148; 62.7%) or less than recommended therapy associated with worse outcomes (88; 37.3%). Overtreatment most commonly implied intensive treatment of an older adult in whom the harms of treatment outweigh the benefits (38; 53.5%) or intensive treatment of a cancer not expected to affect an older adult in his/her remaining lifetime (33; 46.5%).

**CONCLUSION** Undertreatment and overtreatment of older adults with cancer are imprecisely defined concepts. We propose new, more rigorous definitions that account for both oncologic factors and geriatric domains.

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## INTRODUCTION

Older adults make up the growing majority of patients with cancer yet continue to be under-represented in clinical trials.<sup>1,2</sup> This under-representation has led to a lack of knowledge with regard to how risk factors unique to older adults, such as multimorbidity, functional dependency, and frailty, interact with novel treatments studied in trials.<sup>3</sup> Under-representation has also led to a lack of knowledge about how cancer and its treatment affect function and quality of life (QOL), outcomes older adults value as much as, if not more than, survival.<sup>4,5</sup> These knowledge gaps create clinical uncertainty.<sup>6</sup> The terms undertreatment and overtreatment are often used when uncertainty is believed to lead to inappropriate treatment decisions. On one side of the spectrum, physiologically robust older adults who may benefit from intensive medical, surgical, and/or radiation therapies are often precluded

from receiving them on the basis of chronological age alone. On the other side, frail older adults may not tolerate guideline-based treatments that are grounded in evidence from research enrolling predominantly younger patients with minimal comorbidities and good performance status.<sup>7,8</sup>

The prevention of undertreatment and overtreatment of older adults with cancer is more possible now than ever. Significant progress has been made in risk stratifying older patients beyond age and traditional performance status scales (eg, Eastern Cooperative Oncology Group performance status); ASCO and other cancer-focused organizations now recommend a geriatric assessment for all older adults with cancer considering systemic therapy to detect biophysical, functional, and psychosocial impairments that can increase the likelihood of toxicity from cancer therapies.<sup>9</sup> However, no universal consensus definition of

### ASSOCIATED CONTENT

#### Data Supplement Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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## CONTEXT

### Key Objective

The terms undertreatment and overtreatment are often used to describe the mismanagement of older adults with cancer. However, no consensus definition of under- or overtreatment currently exists. We conducted a comprehensive scoping review of the literature to clarify the meanings behind the use of these terms.

### Knowledge Generated

The majority of articles using the terms undertreatment or overtreatment with regard to older adults with cancer do so without explicit definitions, and we found significant variability in the implicit meanings. Survival and surrogate treatment outcomes are overemphasized, while important outcomes like functional status and patient preferences are underemphasized.

### Relevance

The limitations and imprecision in the current concepts of undertreatment and overtreatment carry potentially harmful implications for older adults with cancer. We propose new, more rigorous definitions that synthesize the findings of our review and the current evidence from geriatric oncology. These definitions aim to better match treatment intensity with age-associated vulnerability and align relevant outcomes with patient preferences.

under- or overtreatment exists, and there may be implicit meanings of these concepts that vary across disciplines, providers, and patients. It is critical to identify and clarify these underlying meanings because the terms undertreatment and overtreatment assert a claim: that a given treatment prescribed to an older adult was too little or too much relative to some optimal treatment. Prevention of the undertreatment and overtreatment of older adults with cancer must begin with rigorously defining what constitutes undertreatment and overtreatment.

The objective of this review is to clarify the meanings behind the use of the terms undertreatment and overtreatment as applied to older patients with cancer. To date, no such review exists. We conducted a comprehensive scoping review of the literature to identify articles of older adults with cancer that include these terms. We extracted explicit or implicit definitions to assess for commonalities, differences, and limitations. Finally, we propose more rigorous definitions of undertreatment and overtreatment that are grounded in evidence-based medicine and account for both oncologic factors and geriatric domains.

## METHODS

### Methodology of Scoping Review

To explore the meanings behind the current uses of the terms undertreatment and overtreatment, we conducted a scoping review to map key concepts associated with a topic and clarify definitions.<sup>10</sup> Neither a systematic review nor a meta-analysis were possible given the imprecision in the uses of the terms undertreatment and overtreatment that preclude the combination of outcomes across studies. Rather than analyze the effectiveness of one or more interventions in articles using these terms with a specified set of outcomes, we investigated authors'

consideration of the interventions and outcomes believed to comprise undertreatment and overtreatment in older adults with cancer. To guide our review, we developed an a priori protocol that adheres to the latest standards recommended by the Johanna Briggs Institute and Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews<sup>11,12</sup> (Data Supplement, online only).

### Article Search, Selection, and Data Extraction

We searched PubMed (National Center for Biotechnology Information), Embase (Elsevier), and CINAHL (EBSCO) for records representing cancer studies in older adults that included the terms undertreatment or overtreatment in the title and/or abstract. Although Embase contains some gray literature, we sought only published articles. The searches, carried out on April 28, 2018, were restricted to articles written in English. The search strategies are included in the Data Supplement. Next, C.D. screened the titles and abstracts of all search results for inclusion and exclusion criteria. All types of articles (primary and secondary research articles, including interventional studies, observational studies, reviews, letters to the editor, and news articles), treatments (medical, surgical, and/or radiation therapies), and cancers (solid or hematologic) were included. We excluded studies of patients exclusively < 60 years of age as well as studies that included younger patients but did not specifically delineate a subgroup of older patients. Relevant data from all articles were extracted, including study design, location, type of cancer and treatment studied, outcomes, and article sections where the terms undertreatment and/or overtreatment were used. We surveyed whether each article recommended the geriatric assessment and whether any analyses adequately accounted for geriatric domains.

## Analysis

Articles were identified by C.D. (a geriatrician) that reported explicit definitions of undertreatment and overtreatment. For the remainder, implicit definitions were inferred by examining the terms' surrounding context while incorporating any associated analyses conducted by the authors. A qualitative analysis that was based on grounded theory was then conducted in the following manner.<sup>13</sup> First, definitions were reviewed, and one or more common categories underlying these definitions were derived through an iterative process. Second, the derived subcategories were reviewed for common, underlying categories. Third, a second author (K.P.L., an oncologist) independently repeated these two steps on a randomly selected (by computer algorithm) subset of 50 articles. C.D. and K.P.L. discussed and agreed on the final subcategories and categories that encompassed extracted definitions. Then, C.D. and K.P.L. independently assigned these categories in this subset of 50 articles to assess for inter-rater reliability. Any differences in assignment within this subset were resolved by C.D. and K.P.L. followed by C.D. re-reviewing all remaining articles for accurate assignment of the final categories.

## RESULTS

Figure 1 shows a flow diagram of article inclusion in our review. Our searches returned 3,534 records (PubMed, 1,675; Embase, 1,474; CINAHL, 395). After removal of duplicates, 2,052 records remained. Of these, 1,758 failed to meet the inclusion criteria or met one or more exclusion criteria. The full text of the remaining 294 articles was examined, after which an additional 38 articles were excluded on the basis of not meeting the inclusion criteria, lacking relevance to our topic, or unavailability, which left 256 articles for our analysis.

Table 1 lists the characteristics of the included articles that used the terms undertreatment and/or overtreatment with regard to older adults with cancer (n = 256). Overall, 236 articles used the term undertreatment at least once, 71 used the term overtreatment, and 51 used both terms. Of the 63 primary research articles, the largest proportion was cohort studies (48; 18.8%); of the 193 secondary research articles, the largest proportion was reviews (95; 37.1%). Fifty-five articles (21.5%) focused on multiple cancers or did not specify cancer type, whereas the remainder focused on specific cancer types, including breast (75; 29.3%), lung (30; 11.7%), and colorectal (28; 10.9%), among others. The majority of articles (165; 64.5%) focused on multiple treatments or combinations of treatments (medical, surgical, and/or radiation therapies). Similarly, the majority of articles focused on multiple outcomes (158; 61.7%), whereas 63 (24.6%) focused mainly on survival or surrogates of survival, 32 (12.5%) on decision making, and only 3 (1.2%) on QOL. Eighty articles (31.3%) did not discuss QOL, patient values, and/or patient preferences at any point.

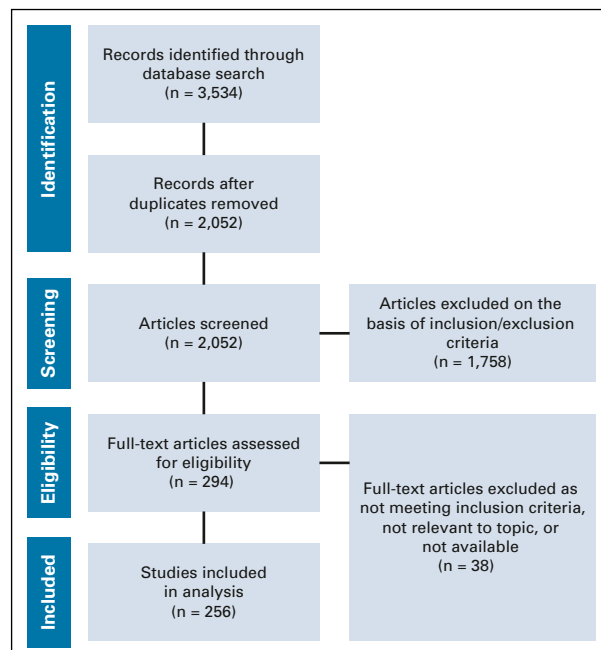


FIG 1. Flow diagram of article inclusion in review.

Fourteen articles (5.5%) included an explicit definition that accompanied their use of the terms undertreatment and/or overtreatment. For the remaining articles, the implicit definitions of undertreatment and overtreatment were inferred from the terms' surrounding context. These explicit and implicit definitions for all articles, as well as the location in each article where the terms were used, are listed in the Data Supplement.

Through qualitative analysis, 12 distinct subcategories emerged from all of the extracted explicit and implicit definitions: eight subcategories that pertained to the definitions of undertreatment and four that pertained to the definitions of overtreatment (Table 2). These subcategories were then synthesized into broader, encompassing categories on the basis of common and distinguishing features. Table 3 lists the distribution of these categories by study and malignancy type. Inter-rater agreement between C.D. and K.P.L. on their independent assignment of these categories within a random subset of 50 articles was 87.1%, with a  $\kappa$ -coefficient of 0.81.

### Categories Underlying the Reviewed Definitions of Undertreatment

Table 2 lists the two broad categories and eight subcategories that emerged from the explicit and implicit definitions of the term undertreatment. In the first broad category, 148 (62.7%) of the 236 articles that included the term undertreatment defined it as prescribing less than a recommended therapy (medical, surgical, radiation, or a combination of these). Authors either used the words less than standard (77; 32.6%), less than guideline or guideline based (23; 9.7%), less than intensive or aggressive (31;

**TABLE 1.** Characteristics of Included Articles

Characteristic	No.	% <sup>a</sup>
No. of articles	256	
Primary research	63	24.6
Cohort study	48	18.8
Qualitative/survey study	4	1.6
Phase II trial	4	1.6
Cross-sectional study	3	1.2
Case report/series	4	1.6
Secondary research	193	75.4
Review	95	37.1
Secondary longitudinal analysis (randomized controlled trial, cohort study, others)	59	23.0
Editorial/news article	15	5.9
Meta-analysis	4	1.6
Letter to the editor	6	2.3
Educational book	3	1.2
Cross-sectional study	7	2.7
Guideline/recommendations	2	0.8
Commentary/conference highlights	2	0.8
Malignancy type		
Breast	75	29.3
Lung	30	11.7
Colorectal	28	10.9
Prostate	27	10.5
Hematologic	18	7.0
Gynecologic	13	5.1
Genitourinary (other than prostate)	10	3.9
Other (multiple, not specified, etc)	55	21.5
Country		
Australia	1	0.4
Austria	1	0.4
Brazil	3	1.2
Canada	6	2.3
China	3	1.2
Czech Republic	2	0.8
Denmark	1	0.4
France	17	6.6
Germany	10	3.9
Italy	18	7.0
Japan	4	1.6
Portugal	2	0.8
Singapore	2	0.8
Spain	4	1.6
Sweden	3	1.2

(continued in next column)

**TABLE 1.** Characteristics of Included Articles (continued)

Characteristic	No.	% <sup>a</sup>
Switzerland	1	0.4
The Netherlands	11	4.3
Tunisia	1	0.4
Turkey	3	1.2
United Kingdom	9	3.5
United States	41	16.0
Not specified (eg, reviews, editorials)	113	44.1
Main intervention/exposure		
Medical (chemotherapy, targeted, etc)	42	16.4
Surgical	16	6.3
Radiation	7	2.7
Multiple or combined	165	64.5
Other (eg, age, comorbidity)	26	10.2
Main outcome		
Main outcomes apparent	129	50.4
Survival	63	24.6
Overall survival	21	8.2
Cancer-specific survival	6	2.3
Multiple or other survival	36	14.1
Decision making	32	12.5
Receipt of treatment (yes/no)	21	8.2
Choice of treatment (type or dose)	11	4.3
Quality of life	3	1.2
Multiple/other	158	61.7

<sup>a</sup>Percentages may not sum to 100 because of rounding.

13.1%), or less than in younger patients (17; 7.2%). These four subcategories all shared the common feature of qualifying undertreatment as less therapy in older adults either in dose, proportion of patients prescribed, or modifications of a surgery or procedure compared with some reference or recommended treatment. The terms used to represent what this recommended treatment was (standard, guideline, intensive) were most often not defined themselves. Nearly half of the articles in this category were review articles (68; 45.9%; [Table 3](#)).

In the second broad category, 88 (37.3%) of the 236 articles using the term undertreatment defined it as less than recommended therapy that is associated with worse outcomes. The four subcategories that were included in this category were similar to the first category in the types of recommended therapy used as a reference (ie, less than standard, less than guideline based, less than intensive, less than younger patients). However, the distinguishing feature for the second category was that undertreatment was not merely less than recommended therapy but that this lesser therapy contributed to worse outcomes compared with a recommended therapy. Seventy-eight of these

**TABLE 2.** Categories and Subcategories of “Undertreatment” and “Overtreatment” That Are Used in the Literature

Category	Articles, No. (%) <sup>a</sup>
Undertreatment (n = 236)	
Less than recommended therapy	148 (62.7)
Less than standard therapy <sup>b</sup>	77 (32.6)
Less than guideline-based therapy <sup>b</sup>	23 (9.7)
Less than intensive therapy <sup>b</sup>	31 (13.1)
Less therapy than in younger patients	17 (7.2)
Less than recommend therapy that is associated with worse outcomes	88 (37.3)
Less than standard therapy that is associated with worse outcomes <sup>b</sup>	54 (22.9)
Less than guideline-based therapy that is associated with worse outcomes <sup>b</sup>	13 (5.5)
Less than intensive therapy that is associated with worse outcomes <sup>b</sup>	9 (3.8)
Less therapy than in younger patients that is associated with worse outcomes	12 (5.1)
Overtreatment (n = 71)	
Intensive treatment of an older adult in whom the harms of treatment outweigh the benefits	38 (53.5)
Intensive treatment where toxicity outweighs benefit	33 (46.5)
Intensive treatment with no proven benefit	5 (7.0)
Intensive treatment of a cancer not expected to affect an older adult in his/her remaining lifetime	33 (46.5)
Intensive treatment of indolent cancers	28 (39.4)
Intensive treatment of cancer in patient with limited life expectancy	5 (7.0)

<sup>a</sup>Percentages may not sum to 100 because of rounding.

<sup>b</sup>The terms standard, guideline based, or intensive were not defined in most cases.

articles (88.6%) defined worse outcomes as worse survival or surrogate measures of survival (Data Supplement).

Many observational cohort studies supported this definition of undertreatment with a primary or secondary analysis (39 [44%] of 88 articles listed in the Data Supplement). These analyses showed that older adults who received a pre-defined recommended therapy had better survival (overall, disease-specific, or surrogate of survival) than older adults who received less than recommended therapy, or alternatively, that compared with younger patients, older patients received lower rates of recommended therapy and had worse survival (in separate analysis). There were variable approaches to account for factors that may have confounded the relationship between the receipt of recommended therapy and survival. Eleven of these 39 studies performed only univariable analyses without any adjustment,<sup>14-24</sup> 16 performed multivariable analyses that adjusted mainly for disease-based factors (eg, tumor stage) but not for any geriatric assessment domains,<sup>25-40</sup> and 12 performed limited adjustment beyond disease-based factors (eg, adjusted for performance status and/or comorbidity but not for other important geriatric assessment domains, such as functional status, mobility, and cognition).<sup>41-52</sup> Toxicity associated with treatment was reported in 3 of these 39 studies. Comments on other analyses that were included in articles but not used as evidence to support undertreatment or overtreatment are listed in the Data Supplement.

### Categories Underlying the Reviewed Definitions of Overtreatment

Table 2 lists the two broad categories and four subcategories that emerged from the explicit and implicit definitions of the term overtreatment. In the first broad category, 38 (53.5%) of the 71 articles that included the term overtreatment defined it as intensive treatment of an older adult in whom the harms of treatment outweigh the benefits. The first subcategory included definitions that referred to treatment with possible benefit but with excessive toxicity that outweighs this benefit (33; 46.5%). This first subcategory often referred to excessive toxicity in a frail or vulnerable older adult whose physiologic reserves could not tolerate intensive therapy. The second subcategory included definitions that referred to treatment that has no proven benefit regardless of the patient's health status (eg, axillary lymph node dissection when sentinel lymph node biopsy is sufficient in women with breast cancer [5; 7.0%]).<sup>53</sup>

In the second broad category, 33 (46.5%) of the 71 articles that included the term overtreatment defined it as intensive treatment of a cancer not expected to affect an older adult in his/her remaining lifetime. The majority of these articles focused on prostate cancer (23; 69.7%; Table 3). Authors focused on either the first component of this definition in the first subcategory—treating an indolent, slow-growing cancer (eg, low-risk prostate cancer [28 articles; 39.4%])—or the latter component of this definition in the second

**TABLE 3.** Distribution of Categories of “Undertreatment” and “Overtreatment” by Study and Malignancy Type  
Category, No. (%)<sup>a</sup>

Type	Undertreatment		Overtreatment	
	1 (n = 148)	2 (n = 88)	1 (n = 38)	2 (n = 33)
Study				
Primary research	43 (29.1)	16 (18.2)	8 (21.1)	4 (12.1)
Review/meta-analysis	68 (45.9)	30 (34.1)	18 (47.4)	9 (27.3)
Secondary longitudinal analysis	21 (14.2)	29 (33.0)	3 (7.9)	14 (42.4)
Other secondary research	16 (10.8)	13 (14.8)	9 (23.7)	6 (18.2)
Malignancy				
Breast	42 (28.4)	30 (34.1)	13 (34.2)	4 (12.1)
Lung	23 (15.5)	7 (8.0)	2 (5.3)	0 (0)
Colorectal	23 (15.5)	5 (5.7)	3 (7.9)	0 (0)
Prostate	9 (6.1)	5 (5.7)	1 (2.6)	23 (69.7)
Hematologic	10 (6.8)	7 (8.0)	6 (15.8)	1 (3.0)
Gynecologic	4 (2.7)	9 (10.2)	1 (2.6)	0 (0)
Genitourinary (other than prostate)	5 (3.4)	3 (3.4)	2 (5.3)	2 (6.0)
Other (multiple, not specified, etc)	32 (21.6)	22 (25.0)	10 (26.3)	3 (9.1)

NOTE. Undertreatment category 1, less than recommended therapy; undertreatment category 2, less than recommended therapy that is associated with worse outcomes; overtreatment category 1, intensive treatment of an older adult in whom the harms of treatment outweigh the benefits; and overtreatment category 2, intensive treatment of a cancer not expected to affect an older adult in his/her remaining lifetime.

<sup>a</sup>Percentages may not sum to 100 because of rounding.

subcategory—treating a patient with limited life expectancy independently of the aggressiveness of their cancer (eg, a patient more likely to die as a result of a comorbidity other than prostate cancer<sup>54</sup> [5 articles; 7.0%]). These subcategories shared the common feature of focusing on the cancer and/or the patient with the cancer, wherein the time to the development of symptoms from the cancer exceeded the expected time to death of the patient. Intensive treatment of the cancer in this circumstance was deemed overtreatment. Although there is some overlap in concepts between the first and second broad categories of overtreatment, the first category focuses more on the harm/benefit ratio of the treatment itself, whereas the second category focuses on the time to benefit of the treatment—a function of the aggressiveness of the cancer and the life expectancy of the patient.

### Geriatric Assessment

Just over half of all included articles advocated for the use of the geriatric assessment to risk stratify older adults for treatment selection (135 [52.7%] of 256; Data Supplement). Fewer advocated for its use to detect age-related vulnerabilities (eg, cognitive impairment, functional dependency) for further management alongside cancer treatment (67; 26.2%).

## DISCUSSION

To our knowledge, this is the first comprehensive scoping review to date that has sought to clarify the meaning of the

terms undertreatment or overtreatment used to describe the management of older patients with cancer. Through our qualitative analysis of reviewed definitions, we derived 12 distinct subcategories of definitions for undertreatment and overtreatment, which coalesced into two categories for undertreatment and two categories for overtreatment. Our review demonstrates that there are limitations and imprecision in the current concepts of undertreatment and overtreatment, and this imprecision carries potentially harmful implications, which we describe next. We conclude by proposing new, more rigorous definitions of undertreatment and overtreatment that synthesize the findings of our review and the current evidence in geriatric oncology.

Articles that defined undertreatment as offering older adults less than recommended therapy correctly argue against age bias in withholding potentially beneficial treatments but understate the limitation that older adults are often not included in the trials used to support these recommended therapies.<sup>2,7,8,55,56</sup> The second category of undertreatment improves upon the first by considering whether less than recommended therapy actually leads to worse outcomes. However, the majority of articles in this second category defined worse outcomes as worse survival, with many focusing on disease-specific survival and surrogate survival measures (eg, progression-free survival).<sup>25,32,41,51</sup> This overemphasis on survival and surrogates raises several issues.

First, vulnerable older patients treated with intensive therapy may actually have higher all-cause mortality as a result of treatment toxicity, even if their cancer-specific mortality is lower.<sup>57</sup> Second, surrogate survival outcomes, such as progression-free survival, may correlate poorly with patient-centered outcomes, such as QOL.<sup>58-60</sup> Third, any improvement in survival may be outweighed by treatment-associated declines in function and QOL. Older adults often value function and QOL just as much as, if not more than, survival, and many may not accept a cancer treatment if it is associated with declines in these outcomes, even if it prolongs life.<sup>4,5,61</sup> This harm/benefit imbalance is magnified when the gains in survival are minimal and the costs to QOL are large.<sup>62-64</sup> There is limited high-quality evidence to inform this balance given the under-representation of vulnerable/frail older adults in trials leading to recommended cancer therapies.<sup>2,65</sup>

Finally, the articles that conducted observational studies showing worse outcomes in older patients treated with less intensive therapy (compared with recommended therapy) did not sufficiently measure and account for the impact of age-related vulnerabilities<sup>21,23,26,29,31</sup> (Data Supplement). Not accounting for geriatric domains such as multimorbidity, cognitive impairment, or functional dependency opens the possibility for significant unmeasured confounding in the association between treatment intensity and outcomes (eg, confounding by indication/contraindication).<sup>66</sup> Vulnerable patients with geriatric domain deficits in addition to their cancer are less likely to be treated with intensive therapies, but their higher mortality may be mediated through these age-related deficits rather than through the receipt of lower intensity cancer treatment.<sup>9,67-71</sup> Indeed, several studies outside this review report decreased benefits and increased harms when intensive guideline-recommended therapies are prescribed to vulnerable older adults in real-world practice.<sup>3,72-74</sup>

The first category of overtreatment denotes a mismatch between the intensity of cancer therapy and the vulnerability of an older patient, whereas the second category defines overtreatment as cancer therapy without benefit in an older patient's remaining lifetime. Both categories highlight distinct, important features of overtreatment but when considered separately, are incomplete definitions. Many articles that used the first category focused on applying recommended intensive treatments (eg, open surgery, stem-cell transplantation, combined therapies) in vulnerable or frail older patients who could not tolerate the burden or toxicity of the treatment.<sup>75-77</sup> However, even lower intensity treatments (eg, localized surgery such as a lumpectomy<sup>78</sup>) can exceed the reduced physiologic reserves of vulnerable or frail older patients and contribute to functional decline and/or death.

Moreover, many articles in the first category failed to advocate for using geriatric assessment to better define

vulnerability in older adults for risk stratification, and even more failed to recommend using geriatric assessment-guided interventions that target reversible causes of vulnerability/frailty.<sup>9,79</sup> Articles using the second category of overtreatment related overtreatment to the better-known concept of overdiagnosis (detecting with a screening test a cancer that will not cause symptoms in a patient's lifetime), and the National Cancer Institute similarly defines overtreatment through linking it with overdiagnosis.<sup>80</sup> However, overtreatment pertains not only to screen-detected malignancies but also to cancers diagnosed from symptoms. In either scenario, clinicians must consider both the aggressiveness of the cancer and the life expectancy of the patient to estimate whether a cancer treatment can confer any benefit in an older adult's remaining lifetime.<sup>9</sup> In addition, providers must weigh the harms of the treatment against the benefits, as reflected in the first category of overtreatment discussed previously.

Examination of the categories that emerged from this review raises important issues with regard to the current understanding of what it means to undertreat or overtreat an older adult with cancer. First, although the majority of articles used these terms without an explicit definition, we identified variability in the implied meanings. Second, an overemphasis on disease-specific and survival measures neglects other risk factors and outcomes important in older adults.<sup>81</sup> Third, nearly a third of articles made no reference to patient values, preferences, and/or QOL, and those that did often did so peripherally to their use of the terms undertreatment or overtreatment.<sup>82-85</sup> A discussion of what outcomes matter most to an individual older patient should come first in defining and avoiding under- or overtreatment.<sup>86,87</sup> Establishment of priorities for an older patient, who may have many comorbidities and functional limitations aside from cancer, can be nuanced and vary from patient to patient.<sup>88</sup> An older patient who values and believes that his/her life can be prolonged by cancer treatment may be willing to tolerate the burden and toxicity of an intensive treatment to achieve this benefit.<sup>5</sup> When facing the same treatment options, a different older patient who prioritizes QOL over quantity of life may view intensive treatment as a net harm, not as a net benefit.

Consequently, the variability in meanings behind undertreatment and overtreatment, the overemphasis on disease-specific and survival measures, and the underemphasis on patient preferences may dangerously lead to overtreatment when trying to avoid undertreatment and vice versa. For example, some clinicians may view that withholding guideline-concordant definitive surgery in a 75-year-old with early-stage breast cancer is undertreating this patient and may elevate her risk of cancer-specific mortality.<sup>89</sup> However, if this 75-year-old is vulnerable with multimorbidity, cognitive, and/or functional deficits, then

she may be at higher risk of other-cause mortality that is unaffected by or even exacerbated by surgery.<sup>78</sup> If the goals of the patient and her family are to preserve function and QOL given her vulnerability and limited prognosis at baseline, then surgery would be overtreatment. Conversely, if this patient is community dwelling, fit, and values survival even with potential tradeoffs, then not offering definitive surgery would be undertreatment.<sup>90</sup> Some clinicians may view that full definitive treatment in this 75-year-old is overtreatment on the basis of a perceived risk of toxicity and/or limited benefit associated with (chronologic) age alone; this view would be uninformed without rigorous assessment of age-related vulnerabilities and a discussion of patient preferences. If such treatment decisions are made, recorded in a database with mainly disease-based measures, and retrospectively analyzed years later by a separate investigator, then any interpretation of under- and overtreatment runs the risk of the same limitations identified in this review.<sup>91</sup> Without a singular theoretical framework and more rigorous, consistent definitions, undertreatment and overtreatment will continue to be applied in an imprecise manner across researchers, clinicians, and patients.<sup>92</sup>

We thus propose new definitions of undertreatment and overtreatment that synthesize the findings of our review and the current evidence in geriatric oncology (Table 4). Although some may challenge the very attempt at forming universally accepted definitions, we believe that this attempt must be made given the variability and harmful implications of the status quo. Our proposed definitions account for both oncologic factors and geriatric domains important in the care of older adults with cancer. We further ground our definitions in the framework of evidence-based medicine, which advocates for the incorporation of the latest best evidence with patient values to optimize decision making.<sup>93</sup> Figures 2A-D illustrate the essential concepts with examples of our definitions.

As an example in applying our definition of overtreatment, the ESOGIA trial compared the use of geriatric

assessment in determining chemotherapy allocation to usual care for older adults with lung cancer.<sup>94</sup> Although older adults in the geriatric assessment arm did not experience an improvement in the primary surrogate outcome of treatment failure-free survival, they received less intense chemotherapy, had less toxicity, and had better QOL, all while maintaining similar overall survival.<sup>95</sup> The trial was deemed negative on the basis of the surrogate outcome. However, it should be interpreted as positive in preventing overtreatment in the older patients who achieved similar survival benefit with less toxicity: a greater net benefit. This more accurate interpretation of the trials' results stems from our more accurate definition of overtreatment and illustrates how our definition can be used not only in practice but also as an outcome to assess in efficacy research studying older adults with cancer.

A limitation of our review was that the requirement of the term undertreatment or overtreatment in our search strategy potentially excluded other relevant articles that discuss related concepts. This specific search strategy was used given that the intent of this scoping review was to clarify the meaning behind the use of the terms undertreatment and overtreatment themselves because these terms are most commonly used to refer to inappropriate management of an older adult with cancer. Our rationale was to select for articles that made these terms an essential focus of their content by placing them in their titles and/or abstracts.

In conclusion, the undertreatment and overtreatment of older adults with cancer are imprecisely defined concepts. We propose new, more rigorous definitions that shift disease-centric criteria to patient-centered criteria, with a broader focus on not only survival but also on function and QOL. Additional research must investigate how cancer and its treatment interact with geriatric domains to affect these three outcomes through both enrolling more older adults in clinical trials and incorporating geriatric measures in well-designed observational studies.<sup>55</sup> This evidence will better delineate the harms and benefits of cancer

**TABLE 4.** Newly Proposed Definitions of Undertreatment and Overtreatment in Older Adults With Cancer

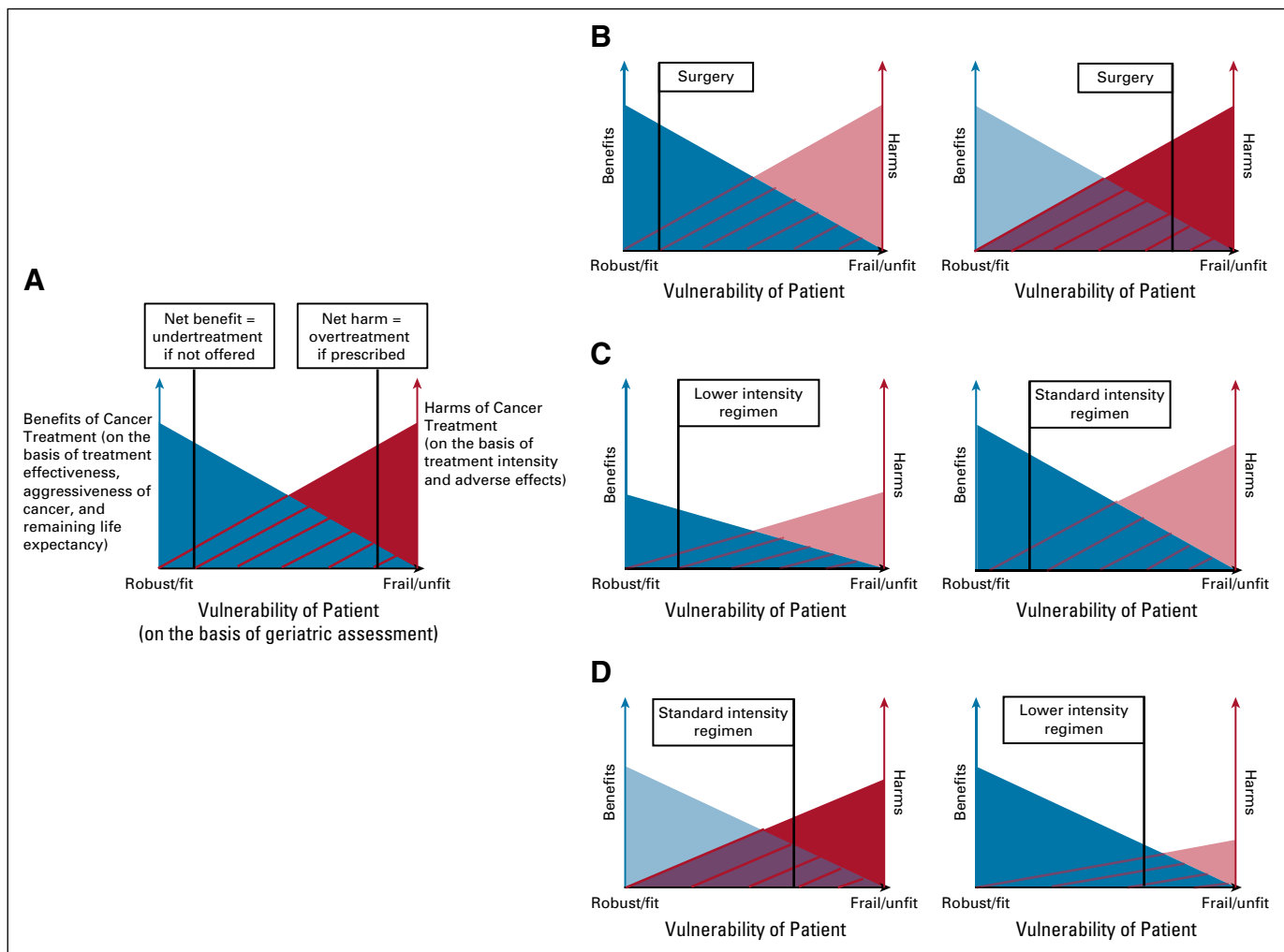
Term	Definition
Undertreatment	Use of less intensive <sup>a</sup> cancer treatment in a fit <sup>b</sup> older adult who would otherwise derive a greater net benefit <sup>c</sup> from more intensive cancer treatment and/or Not providing nononcologic interventions to deficits in geriatric domains <sup>b</sup> regardless of what cancer therapy is chosen
Overtreatment	Treatment of a cancer in an older patient that would not likely lead to symptoms in his/her remaining lifetime or Intensive treatment of a cancer in a vulnerable <sup>b</sup> older patient in whom there would be a greater net benefit <sup>c</sup> from less intensive therapy

<sup>a</sup>Some reduction in a recommended/standard treatment regimen normally used in younger, fit patients.

<sup>b</sup>Assessment and management of geriatric domains in accordance with ASCO's guideline for geriatric oncology.<sup>9</sup>

<sup>c</sup>Benefits as jointly defined by the physician and patient outweigh the similarly defined harms resulting from the cancer treatment.





**FIG 2.** Graphical illustration of essential concepts of proposed definitions of undertreatment and overtreatment. (A) General graph of relationships among benefits of cancer treatment, harms of treatment, and vulnerability of older patient. Benefits of cancer treatment are a function of the effectiveness of the treatment, the aggressiveness of the cancer, and the remaining life expectancy of the patient. Harms of a particular treatment are a function of treatment intensity and adverse effects. Vulnerability is a function of geriatric assessment deficits (eg, cognitive impairment, functional dependency). As patient vulnerability increases, treatment benefits decrease and harms increase. For a given vulnerability on the x-axis, the blue shading represents a treatment where the benefits outweigh the harms (net benefit = undertreatment if not offered). For more severe vulnerability on the x-axis, the red shading represents a treatment where the harms outweigh the benefits (net harm = overtreatment if prescribed). The more intensive color shading in the next figure panels helps to illustrate net harm v net benefit for a given patient and treatment. Individual patient preferences should inform the balance between benefits and harms of a given treatment. (B) The left panel shows an example of undertreatment when considering definitive surgery in a fit older patient: A 75-year-old community-dwelling female with few comorbidities has early-stage breast cancer and values survival even with tradeoffs but is not offered definitive cancer surgery on the basis of her age alone. The right panel shows an example of overtreatment when considering definitive cancer surgery in a vulnerable older patient: A 75-year-old female nursing home resident with limited life expectancy has early-stage breast cancer and values quality of life over survival but is recommended to undergo definitive surgery that leads to an irreversible decline in function.<sup>78</sup> (C) Example of undertreatment when considering variable intensities of chemotherapy in a fit patient: A 75-year-old male with intact cognitive and physical function has multiple myeloma and values survival even with tradeoffs but is treated with a lower intensity chemotherapy regimen on the basis of age alone (left panel) when a standard intensity regimen (right panel) offers greater prolongation of life.<sup>96</sup> (D) Example of overtreatment when considering variable intensities of chemotherapy in a vulnerable patient: A 75-year-old male with advanced osteoarthritis and sarcopenia has gastroesophageal cancer but is prescribed a higher intensity chemotherapy regimen (left panel) when a lower-intensity regimen (right panel) offers similar survival benefit with less toxicity.<sup>97</sup>

treatments in older adults. However, application of this evidence to treatment decisions—and in approaching decisions where evidence is limited—requires new standard criteria for undertreatment and overtreatment to

maximize net benefit and avoid net harm. Our proposed definitions seek to meet this need by better matching treatment intensity to age-related vulnerability and aligning anticipated outcomes with patient values.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

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#### **AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**

##### **Defining Undertreatment and Overtreatment in Older Adults With Cancer: A Scoping Literature Review**

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to [www.asco.org/rwc](http://www.asco.org/rwc) or [ascopubs.org/jco/authors/author-center](http://ascopubs.org/jco/authors/author-center).

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians ([Open Payments](#)).

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