Exploring Cost-Effectiveness of the Comprehensive Geriatric Assessment in Geriatric Oncology: A Narrative Review

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Simple Summary: The Comprehensive Geriatric Assessment is a multidimensional and multidisciplinary evaluation designed for elderly patients with the goal of structuring tailored care and follow-up. Despite the known benefits of this approach, the Comprehensive Geriatric Assessment is not universally applied to elderly cancer patients due to economic and practical barriers. This narrative review aims to investigate the cost-effectiveness of the Comprehensive Geriatric Assessment adopted in geriatric oncology. The results revealed a lack of research on the topic, but recurrent cost-saving effects of this approach in geriatric oncology settings were highlighted—suggesting a positive cost-effectiveness ratio. Further structured research with comprehensive economic evaluations is needed to confirm these findings.

Abstract: The Comprehensive Geriatric Assessment (CGA) and the corresponding geriatric interventions are beneficial for community-dwelling older persons in terms of reduced mortality, disability, institutionalisation and healthcare utilisation. However, the value of CGA in the management of older cancer patients both in terms of clinical outcomes and in cost-effectiveness remains to be fully established, and CGA is still far from being routinely implemented in geriatric oncology. This narrative review aims to analyse the available evidence on the cost-effectiveness of CGA adopted in geriatric oncology, identify the relevant parameters used in the literature and provide recommendations for future research. The review was conducted using the PubMed and Cochrane databases, covering published studies without selection by the publication year. The extracted data were categorised according to the study design, participants and measures of cost-effectiveness, and the results are summarised to state the levels of evidence. The review conforms to the SANRA guidelines for quality assessment. Twenty-nine studies out of the thirty-seven assessed for eligibility met the inclusion criteria. Although there is a large heterogeneity, the overall evidence is consistent with the measurable benefits of CGA in terms of reducing the in-hospital length of stay and treatment toxicity, leaning toward a positive cost-effectiveness of the interventions and supporting CGA implementation in geriatric oncology clinical practice. More research employing full economic evaluations is needed to confirm this evidence and should focus on CGA implications both from patient-centred and healthcare system perspectives.

Keywords: CGA; older adults; geriatric oncology; cost-effectiveness
1. Introduction

Conceived in the 1960s, the Comprehensive Geriatric Assessment (CGA) is “a multidisciplinary process which includes assessment and management of assessed need” of older patients in relation to “medical, social and functional needs”, ending in “the development of an integrated/coordinated care plan to meet those needs” [1]. The CGA comprises different scales to evaluate each health dimension, and single geriatric screening tools are often adopted as alternatives to a full CGA, enabling a brief CGA [2,3]. The CGA has a strong prognostic value and is essential to identifying older adults at risk of a disability. Thus, it is considered a fundamental component of geriatric care [4].

In oncology, the assessment of a patient’s Performance Status (PS) is crucial for the treatment decision and prognosis estimation [5]. The PS predicts the treatment benefits and the risk of toxicity, and it is commonly required for patient enrolment in clinical trials [6]. Among the different PS scales, the Eastern Cooperative Oncology Group PS (ECOG PS) and the Karnofsky PS (KPS) scores are perhaps the most widely adopted tools [6,7]. However, ECOG PS and KPS are not sensitive enough to identify the functional limitations and essentially lose their prognostic value in older patients [8,9]. Instead, the CGA is more accurate in defining the actual degree of fitness of older patients. It allows to properly categorise patients as fit, vulnerable or frail, which, in turn, is supposed to help oncologists make more appropriate treatment decisions.

The CGA typically comes with recommendations/interventions that, by tackling the identified issues (e.g., depression, cognitive impairment, delirium, depression, malnutrition, sleep disorders, social issues, etc.), optimise a patient’s health status, help to regain an active treatment for some of the older patients [10–12] and may also increase a patient’s tolerance to anticancer treatments [13,14].

According to the International Society of Geriatric Oncology (SIOG), the CGA represents the gold standard for (a) defining a prognosis and the ability to withstand cancer treatments, (b) exploring the multiple aspects that define the complexity of frail older persons and (c) designing person-tailored interventions [2]. Similarly, the European Society for medical Oncology (ESMO) [15], the European Society of Surgical Oncology (ESSO) [16], the American Society of Clinical Oncology (ASCO) [17], the National Comprehensive Cancer Network (NCCN) [18], the American College of Surgeons (ACS) [19,20] and the Italian Society of Geriatrics and Gerontology (SIGG) [2] have also recommended the adoption of CGA in older cancer patients (see Table 1).

Table 1. Recommendations in the CGA by scientific associations.

| Proponents                                      | Target Population                                      | Recommendations                                                                 |
|------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------------------------------|
| The International Society of Geriatric Oncology (SIOG) [21,22] | Cancer patients aged 70 or older                      | - adoption of CGA with further interventions and follow-up                      |
|                                                 |                                                        | - use of screening tools to identify those patients who need CGA and multidisciplinary approach, when facing a busy clinical practice |
|                                                 |                                                        | - the preferred screening tool may depend on the clinical situation             |
| The European Society for Medical Oncology (ESMO) [15] | Patients aged 70 or older with diffuse large B-cell lymphoma (DLBCL) | - CGA is recommended to aid patient’s categorisation into fit, vulnerable and terminally ill patients |
| The American Society of Clinical Oncology (ASCO) [17] | Cancer patients aged 65 or older receiving chemotherapy | - CGA results should lay the basis of an integrated and individualised care plan |
|                                                 |                                                        | - clinicians should consider CGA results when recommending chemotherapy         |
|                                                 |                                                        | - the information from CGA should be provided to patients and caregivers to guide treatment decision making |
| The National Comprehensive Cancer Network (NCCN), U.S.A. [18] | Older cancer patients                                | - implementation of pre-treatment evaluation using CGA when there are concerns about the patient’s ability to tolerate treatment or when issues are identified by a geriatric screening tool |
|                                                 |                                                        | - assessment using a geriatric screening tool only, when there are no concerns regarding a patient’s ability to tolerate therapy |
|                                                 |                                                        | - CGA should inform targeted interventions and a coordinated plan for cancer treatment |
Table 1. Cont.

| Proponents | Target Population | Recommendations |
|-------------|-------------------|-----------------|
| The Italian Society of Geriatrics and Gerontology (SIGG) [2] | Cancer patients aged 65 or older | - CGA should be performed in all patients with cancer aged 65 or older  
- as a second choice (whenever resources are limited), adoption of a ‘two-step approach’ (screening to select patients who need CGA)  
- a closer interaction between geriatricts and oncologists (or haematologists) should take place to optimise the approach to cancer patients  
- CGA should be performed by a trained geriatrician with the ability to detect and treat impairments in the different domains, possibly calling into play additional health professionals as needed |
| European Society of Surgical Oncology (ESSO) [16] | Patients aged 70 or older with rectal cancer | - CGA and multidisciplinary evaluation to identify the main predictors of frailty and postoperative complications such as functional status, nutritional status and comorbidities |
| American College of Surgeons (ACS) (and the American Geriatrics Society—AGS) [19,20] | Older cancer patients undergoing oncological surgery | - a preoperative frailty assessment is recommended for all older patients who are candidates to an oncological surgical procedure  
- risk assessment for older patients; management of geriatric domains in the perioperative period, postoperative period and after discharge |

To what extent the CGA has an impact on oncologists’ decisions was studied by Chaïbi and colleagues [23], Girre and colleagues [24] and Marenco and colleagues [25]. These authors found that the CGA affected treatment decisions in a percentage of cases ranging between 21% and 49% [23–26]. Other studies have shown that incorporating the CGA in the management of older patients with cancer (i) improves clinical outcomes by helping select the most appropriate therapy [27], (ii) promotes the inclusion of patient preferences in the decision-making process [28–30], (iii) improves communication between oncologists and patients [28–30], (iv) reduces the risk of over- and undertreatment [31], (v) enhances treatment tolerance and completion [32] and (vi) predicts the frequency of hospitalisation and long-term care for older cancer survivors [33].

The CGA is also beneficial in terms of reducing the mortality, disability and institutionalisation of community-dwelling older people, allowing for the preservation of physical function, lower healthcare utilisation and reduced hospitalisations [34,35]. Although the majority of cancer patients are in the geriatric population [36–38], and despite the reported benefits of the CGA in the geriatric oncology setting, the CGA is not universally applied in older patients due to the lack of workforce (primarily of geriatricians); economic, logistical and practical barriers (e.g., time-consuming) [35] and because of the limited appreciation of the value of the CGA by oncologists. Gladman and colleagues (2016) referred to this issue as “a know-gap” as a way to express the uncertainty in adopting the CGA in specific settings, including clinical oncology [39]. Indeed, since most healthcare systems ultimately only have very limited resources available, showing that the CGA is cost-effective is necessary for it to become the standard of care [40]. Only a few trials have evaluated the costs and the impact of the CGA, resulting in tenuous evidence of its cost-effectiveness [41]. With some exceptions, the available studies suggest that the CGA and the corresponding geriatrics interventions are effective without raising the total cost of care [41]. The review by Fox and colleagues [42] showed that the cost of care in an acute geriatric unit was significantly lower than those of the usual care [42], and two studies concluded there was a reduction in the costs associated with the CGA for many of the hospital-based services analysed [43,44]. A recent RCT of geriatric co-management combined with an interdisciplinary transitional care intervention for frail older patients who had unplanned admissions to internal medicine services in Argentina showed a reduction in 30-day hospital readmissions and emergency department (ED) visits 6 months after discharge in the intervention arm [45]. The cost-effectiveness analysis of the Elder-Friendly Approaches to the Surgical Environment (EASE) Intervention for the emergency abdominal surgical care of older adults [46] conducted by Hofmeister and colleagues suggested that the EASE intervention was associated with a reduction in costs and no change in Quality-Adjusted Life Years (QALYs) [47]. On the other hand, Parker and colleagues [1] concluded that the available studies were lacking a “broader view” meaning an analysis of the direct costs (i.e., staff and resources)
but, also, of the subsequent costs (e.g., community health and social care costs) and of the costs for patients and the wider society [1].

In this review article, we aimed at investigating the cost-effectiveness of the CGA in a geriatric oncology setting.

2. Methods
2.1. Search Strategy and Selection Criteria
2.1.1. Data Sources
This review was based on a search of the PubMed and Cochrane databases for full papers and articles without restrictions based on the year of publication. The review search took place in between June 2021 and January 2022.

After duplicate exclusion, the article titles and abstracts were screened. The full texts were then screened and selected. The study characteristics and information were extracted from the selected papers. The SANRA scale for the quality assessment of narrative review articles was used to evaluate the review, adopting the revised version of the scale [48]. The revised SANRA scale is composed of six items rated from 0 (low standard) to 2 (high standard), with 1 as an intermediate score. The items cover: an explanation of the review’s importance (item 1) and statement of the aims (item 2) of the review, the description of the literature search (item 3), referencing (item 4), scientific reasoning (item 5) and a presentation of the relevant and appropriate endpoint data (item 6). Our review adopted an objective and systematic approach in the selection and analysis of the studies.

2.1.2. Search Terms
- (comprehensive geriatric assessment OR (comprehensive geriatric assessment AND cancer) OR (comprehensive geriatric assessment AND oncology) OR (geriatric assessment AND cancer) OR (geriatric assessment AND oncology) OR (geriatric evaluation AND cancer) OR (geriatric evaluation AND oncology) OR (geriatric evaluation management AND cancer) OR (geriatric evaluation management AND oncology) OR (geriatric co-management AND cancer) OR (geriatric co-management AND oncology) OR (geriatric co-management) OR (geriatric intervention AND cancer) OR (geriatric intervention AND oncology)) AND (cost-effectiveness OR cost OR expenditure OR cost-utility OR utility-analysis);
- (((comprehensive geriatric assessment AND cancer) OR [geriatric comanagement AND cancer] OR [geriatric comanagement AND oncology]) ((comprehensive geriatric assessment AND oncology) OR [geriatric assessment AND cancer] OR [geriatric assessment AND oncology] OR [geriatric evaluation management AND cancer] OR [geriatric evaluation management AND oncology] OR [geriatric evaluation management AND cancer] OR [geriatric co-management AND oncology] OR [geriatric intervention AND cancer] OR [geriatric intervention AND oncology]) AND (length of stay OR LOS) OR (readmission) OR (falls) OR (complications) OR (emergency department);
- (((comprehensive geriatric assessment) OR (geriatric assessment) OR (geriatric comanagement) OR (geriatric co-management) OR (geriatric evaluation management)) AND (cost-effectiveness OR cost OR expenditure OR cost-utility OR utility-analysis)) OR (geriatric intervention) AND toxicity).

2.1.3. Study Eligibility Criteria
To select the studies, as the eligibility criteria, we set (a) the focus on older cancer patients (60 years or older), both sexes, with a diagnosis of cancer and cared for in geriatric oncology settings, or oncology or surgery, or included in heterogeneous geriatric populations in a medical or surgical setting (with a consistent rate of older patients with cancer in the study population); (b) with the implementation of a full CGA or a brief CGA with at least one CGA tool and (c) the recurrence of the cost measures related to the adoption of the CGA (i.e., costs and/or resources required for the management of older patients).
and/or the presence of measures for the effectiveness of the CGA intervention and/or cost-sensitive outcomes (i.e., outcomes with cost-effectiveness implications).

Moreover, such studies were retrospective, prospective cohorts, observational or interventional in nature, with at least 35 included patients.

The records were screened for inclusion based on predefined criteria. The papers were excluded if they concerned:

- Editorials, protocols, score creation studies, ongoing registered trials or completed trials without available results;
- Studies without a specific focus on older adults (i.e., age < 60 years or no data about old age participants);
- Studies without a cancer population or without a reported percentage of cancer patients in the study cohort;
- Studies without measures of the cost-effectiveness or cost-sensitive measures;
- Nursing home patients/patients receiving home care;
- Studies enrolling less than 35 patients.

2.1.4. Analysis of Studies

The studied identified were analysed according to the number and characteristics of the participants (i.e., age, cancer site, stage, therapy and frailty); the study design; the type of CGA and geriatric interventions; the main effects of the interventions and the reported measures of effectiveness suitable for cost-effectiveness or the cost-effectiveness measures when available.

For each study, the (cost-)effectiveness measures reported were classified as (i) cost-sensitive measures (measures of patient health conditions leading to cost-increasing or cost-decreasing effects) and/or (ii) measures of the effectiveness of the CGA intervention (with an estimation of the costs in two studies). The cost-effectiveness propensity of each measure was assessed—that is, the propensity of that measure to sound cost-effective in light of the results obtained in a specific study. Each measure was classified as “positive” when leading to implications that improve the patient health status with a cost-saving or cost-decreasing effect. Conversely, the term “negative” was given to measures that increase the costs. The term “neutral” depicts the measures that present neither positive or negative implications with respect to the cost trend or resource exploitation.

The reason for a qualitative assessment of the propensity lies in the lack of cost-effective measures or cost calculations for the majority of the studies, preventing a true quantitative cost-effective evaluation.

3. Results

3.1. Identification of Relevant Studies

The literature search yielded 8613 potentially relevant papers, with 142 duplicates that were removed. After the removal of the duplicate records, protocols, ongoing studies—as for two conference abstracts [49–51], editorials and records without relevance to the research question, either for their research focus or because they utilised the CGA in non-oncological settings—from abstract and full-text screening, a total of 37 records were assessed for eligibility in the review, including 5 records retrieved during a manual search (Figure 1).

A large number (8613) of articles were identified from the database searches, and 16 additional articles were identified by exploring their bibliographies and by a manual search.

Out of the 37 eligible studies, two studies were not included due to the characteristics of interventions [52,53], two studies were not included because it was not possible to identify the percentage of cancer patients [45,54], two studies were excluded because the number of cancer patients included was very low [46,55] and another two studies were excluded due to nonexplicit criteria for patient inclusion concerning age [56] or the inclusion of patients of all ages [57].
In the end, 29 studies were identified for the review: 24 retrieved from the databases and five from citation searching or the manual search. Twenty-six full-text studies and three conference abstracts showed the results of completed trials [58–60]. All extracted data from the selected articles were categorised according to the study design, study participants and measures of cost-effectiveness.

The literature we found with valuable measures for the cost-effectiveness of the CGA implemented in older cancer patients consisted of 29 studies.

Among the identified studies, there were 15 RCTs [58,59,61–73], 6 observational cohort studies [74–79], 3 before-and-after studies [80–82], 2 pilot studies [60,83], 1 descriptive comparison study [84], 1 prospective observational study [85] and 1 secondary analysis study (of RCT) [86].

Among the studies, 13 were carried out in surgical settings (Table 2) and 16 in medical settings (Table 3). In Tables 2 and 3, we list the details of the studies retrieved.
Table 2. Studies conducted in surgical settings, main features and results.

| Authors | Participants | Type of Study | CGA and Geriatric Interventions | Effectiveness Measures Suitable for Cost-Effectiveness | Main Effect of CGA and Geriatric Interventions | Cost-Effectiveness Propensity |
|---------|--------------|---------------|--------------------------------|--------------------------------------------------------|-----------------------------------------------|------------------------------|
| Nipp et al., 2022 [72] | 14 patients (perioperative) | Type of cancer: CRC (79.7%) | Random assignment to PERI-OP or usual care. Patients assigned to PERI-OP met with a geriatrician preoperatively and postoperatively. Geriatricians communicated findings to surgical oncology teams or (after surgery) to inpatient teams. | Postoperative LoF | In preoperative analyses, PERI-OP patients had shorter postoperative LoF (5.90 vs. 8.21 days, \( p = 0.004 \)), with non-significantly lower rates of postoperative ICU use and 90-day readmissions. | Positive Neutral Neutral |
| Janssen et al., 2019 [80] | 81 patients | Type of cancer: CRC (elective surgery) | A structured multidisciplinary prehabilitation program prior to surgery. PEERS. The program included CGA, nutrition supplementation, resistance training, optimization of cardiac risk for operation, optimization of the discharge process to avoid institutionalization. The control group did not benefit of PEERS program. | QoL LoF | PEERS group had significant improvement in median EQ-SD (0.70 pre-surgery to 0.80 6-months’ post-surgery, \( p = 0.01 \)). After multivariate analysis, average LoF in PEERS group was 6.9 days shorter (\( p = 0.018 \)) after adjusting for modality of surgery and complications, representing a cost-saving of USD 11,850 per patient. | Positive Neutral Neutral |
| Koh et al., 2021 [81] | 310 patients | Type of cancer: CRC (elective surgery) | Geriatric co-management of care with pre-operative (elective Rapid Fitness Assessment) and postoperative evaluations. | Adverse surgical events | CD adverse surgical outcomes within 30 days of surgical treatment did not differ between groups. A higher proportion of patients in the geriatric co-management group were discharged home with home supportive services (10.8% vs. 15.4%, \( p = 0.001 \)). In fully adjusted model, geriatric co-management was significantly associated with reduced 90-day mortality. | Neutral Negative Neutral |
| Shafrakni et al., 2020 [76] | 392 patients | Type of cancer: different malignant neoplasms (and different surgical procedures) | Geriatric co-management of care with pre-operative (elective Rapid Fitness Assessment) and postoperative evaluations. | Severe postoperative complications | Despite at increased risk, MDT patients did not suffer more postoperative CDIII-V complications than non-MDT patients (14.5% vs. 12.6%, \( p = 0.46 \)). Control group was discharged independently at home more often than MDT patients. | Neutral Neutral Neutral |
| van der Vlies et al., 2020 [78] | 433 patients | Type of cancer: MDT patients (75%), non-MDT patients (25%) | Intervention: extended preoperative CGA. MDI estimated the risk of a surgical procedure and when patients were considered eligible for surgery, a prehabilitation program was initiated based on comorbidity and frailty characteristics. Control group: no preoperative MDI approach. | In-hospital LoF | The prehabilitation group had a higher burden of comorbidities and was more physically and visually impaired at baseline. No effect of prehabilitation on LoF, readmissions, unplanned ICU admissions and KU in ICU. | Neutral Neutral Neutral |
| Jansson et al., 2019 [80] | 627 patients | Type of cancer: CRC (79.7%) | Prehabilitation program received interventions to improve physical health, nutritional status, factors of frailty and preoperative anaemia prior to surgery. During the outpatient visit, a nurse practitioner and a physiotherapist re-evaluated patient global health, fitness and frailty. The control group was not pre-habilitated. | Delirium | The prehabilitation group had a higher burden of comorbidity and was more physically and visually impaired at baseline. No effect of prehabilitation on LoF, readmissions, unplanned ICU admissions and KU in ICU. | Neutral Neutral Neutral |
| Taranca-Santahelma et al., 2019 [79] | 203 patients (in intervention group) | Type of cancer: CRC (elective surgery) | Retrospective analysis. | Delirium | At adjusted logistic regression analysis, prehabilitation significantly reduced the incidence of delirium. No effect was observed for postoperative complications, institutionalisation and short-term mortality. | Positive Neutral Neutral |

**Type of Study:** RCT (Randomized Controlled Trial)

**Effectiveness Measures:**
- Postoperative LoF (Length of Stay after surgery)
- QoL LoF (Quality of Life after surgery)
- ICU admission
- Hospital readmissions
- Delirium
- Number of postoperative complications

**Main Effect:**
- Postoperative LoF: In preoperative analyses, PERI-OP patients had shorter postoperative LoF (5.90 vs. 8.21 days, \( p = 0.004 \)), with non-significantly lower rates of postoperative ICU use and 90-day readmissions.
- QoL LoF: PEERS group had significant improvement in median EQ-SD (0.70 pre-surgery to 0.80 6-months’ post-surgery, \( p = 0.01 \)). After multivariate analysis, average LoF in PEERS group was 6.9 days shorter (\( p = 0.018 \)) after adjusting for modality of surgery and complications, representing a cost-saving of USD 11,850 per patient.
- Adverse surgical events: CD adverse surgical outcomes within 30 days of surgical treatment did not differ between groups. A higher proportion of patients in the geriatric co-management group were discharged home with home supportive services (10.8% vs. 15.4%, \( p = 0.001 \)). In fully adjusted model, geriatric co-management was significantly associated with reduced 90-day mortality.
- Severe postoperative complications: Despite at increased risk, MDT patients did not suffer more postoperative CDIII-V complications than non-MDT patients (14.5% vs. 12.6%, \( p = 0.46 \)). Control group was discharged independently at home more often than MDT patients.
- In-hospital LoF: The prehabilitation group had a higher burden of comorbidity and was more physically and visually impaired at baseline. No effect of prehabilitation on LoF, readmissions, unplanned ICU admissions and KU in ICU.
- Delirium: The prehabilitation group had a higher burden of comorbidity and was more physically and visually impaired at baseline. No effect of prehabilitation on LoF, readmissions, unplanned ICU admissions and KU in ICU.

**Cost-Effectiveness Propensity:**
- Positive Neutral Neutral
- Neutral Neutral Neutral
- Positive Neutral Neutral
- Neutral Neutral Neutral
- Negative Positive Neutral
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- Neutral Neutral Negative
The interventional group had shorter mean LoS compared to the control group. No statistically significant differences between intervention and control group for hip fractures (19% vs. 31%) or median age (56% vs. 6%).

Severity of postoperative complications

In the secondary analyses, a statistically significant difference in favour of the intervention in terms of lower CD grade III–IV complications (p = 0.005) was found. No statistically significant differences between intervention and control group for CD grade II–V complications (66% vs. 75%) or 30-day mortality (9% vs. 5%).

No differences in term of LoS between groups. No statistically significant differences between intervention and control group for hip fractures (19% vs. 31%) or median age (56% vs. 6%).

Mean age: 78.6 years

Female: 51%

≥ 65 years

75 years

≥ 70 years

80 years

LoS reductions did not reach statistical significance, although a trend reduction was seen indicating possibly greater reduction with advancing age.

No statistically significant difference in term of medical complications (the reduction of LoS could reflect the prevalence of these).

No statistically significant difference in term of medical complications (the reduction of LoS could reflect the prevalence of these).

Positive

Neutral

Neutral

Neutral

Neutral

Neutral

Neutral

Neutral

Positive

Positive

Positive

Negative

Positive

Neutral

Neutral

Neutral

Positive

Positive

Positive

Positive

Neutral
### Table 2. Continued.

| Authors          | Participants | Type of Study | CGA and Geriatric Interventions | Effectiveness Measures Suitable for Cost-Effectiveness | Main Effect of CGA and Geriatric Interventions | Cost-Effectiveness Propensity |
|------------------|--------------|---------------|--------------------------------|-------------------------------------------------------|-----------------------------------------------|-----------------------------|
| Hempenius et al., 2013 [63] | 260 frail patients ≥ 75 years Mean age: 77 years Female: 77% Type of cancer: solid cancers (elective surgery) - 148 patients in the intervention group - randomisation stratified by cancer type - Frailty: GFI ≥ 3 | RCT | Geriatric liaison intervention to prevent PoD pre-operative CGA by a geriatric team, individual treatment plan, daily visits by a geriatric nurse during the hospital stay and advice on emerging medical problems. The intervention focused on best supportive care and the prevention of delirium. Control group: standard care (additional geriatric care was only provided at the request of the treating physician). | LoS | No significant difference between the groups in most aspects of the SF-36 scale to estimate QoL, although intervention group did not report significantly lower bodily pain at discharge than at admission compared with the usual-care group (OR: 0.49, 95% CI: 0.28–0.82). Neutral Positive |
| Lund et al., 2021 [67] | 142 frail patients ≥ 75 years Mean age: 75 years Female: 43% Type of cancer: stage II–IV CRC (receiving adjuvant (58%) or first-line palliative (42%) CT) - Frailty: G8 ≤ 3 - 71 patients in intervention group | RCT | CGA-based intervention: CGA at the start of CT, follow-up after 2 months or more frequently if needed. Interventions included medication changes (29%), nutritional therapy (51%), physiotherapy (39%), psychotherapy (39%), and DDI); final multidisciplinary medication review by the clinical pharmacist and a geriatrician team (recommendations to reduce ADE risk and ADE risk). A not significant trend was observed for a lower incidence of PoD between the intervention and usual-care group as well as for severity of PoD. This was a significant difference in term of return to preoperative living situation and care in favour of the intervention group, as opposed to the care dependency. | ADEs, CT completion | Grade 3–4 toxicity occurred in 20% of patients from the control arm and in 26% of patients from the CGA arm (p = 0.156), 20% in the intervention group and 38% in the control group discontinued CT due to toxicity (p = 0.175). More patients from the CGA arm completed the scheduled CT compared with controls (43% vs. 28%, p = 0.0344). Neutral Positive |
| Mohle et al., 2021 [62] | 718 frail patients ≥ 75 years Mean age: 77.2 years Female: 43% Type of cancer: inoperable advanced (stage III-IV) solid cancer or lymphoma (starting a new treatment regimen with a high risk of toxic effects within 4 weeks) - Frailty: at least one impaired CGA domain other than PP - 349 patients in intervention arm. | RCT | Intervention (CGA and CGA-guided management integrated into oncology care): patients completed CGA, oncologists received a tailored CGA summary and management recommendations. Usual care: patients completed CGA, no CGA summary or management recommendations were provided to oncologists (only alerts for significantly impaired scores on depression and cognitive screening were sent). | ADEs, PP, Falls | A lower proportion of patients in intervention group had grade 3–4 ADEs compared with usual care group (15% vs. 23%), with a reduced risk of ADEs (p = 0.0102). Patients in the intervention group had fewer falls (21% vs. 25%) with lower risk of having new falls (p = 0.0351) and had more medications discontinued (p = 0.045), reducing PP. Positive |
| Choukroun et al., 2021 [85] | 51 frail outpatients ≥ 75 years Mean age: 81.1 years Female: 55% Type of cancer: not-hematologic solid cancers [breast (27%), CRC (16%), metastatic cancer (42%). - patients with G8 score ≤ 34 - median number of chronic comorbidities (including primary cancer) was 45 [high blood pressure (39%), dyslipidaemia (29%), chronic renal failure (22%), heart failure (20%) and type 2 diabetes (14%)]. | Prospect. observational study | Five-stage process (outpatient): preparation phase; face-to-face pharmaceutical consultation with the patient; CGA performed by an anesthesiologist and a geriatrician (geriatric tools, physical examination); pharmaceutical medication analysis (PIM, DDP, and DDI); final multidisciplinary medication review by the clinical pharmacist and a geriatrician team (recommendations to reduce DDP and optimise prescriptions). After the medication review, the proposals for prescription modification were sent to GPs and oncologists. | PIM, ADE risk PP | A significant decrease was observed in prevalence of PIM use and ADE risk. A not significant trend was observed for a lower number of medications. Positive |

Abbreviations: CD: Clavien-Dindo; CGA: Comprehensive Geriatric Assessment; CRC: Colorectal Cancer; EQ-5D: EuroQol-5 Dimension; G8: Geriatric 8; GFI: Groningen Frailty Indicator; GS: CGA-based care; GI: Gastrointestinal; ICU: Intensive Care Unit; ISAR: Identification of Seniors At Risk (questionnaire); LoS: Length of Stay; MDT: Multidisciplinary team; OS: Overall Survival; RCT: Randomised Controlled Trial; PEERS: Programme for Enhanced Elderly Recovery; PERI-OP: Perioperative geriatric intervention; PoD: Postoperative Delirium; QoL: Quality of Life; 6-CIT: 6-Item Cognitive Impairment Test. White rows: cost-sensitive measures (measures of patient health conditions leading to cost-increasing or cost-decreasing effects); grey rows: measures of effectiveness of CGA intervention (with estimation of costs in two studies [81,86]).

### Table 3. Studies conducted in medical settings, main features and results.

| Authors            | Participants | Type of Study | CGA and Geriatric Interventions | Effectiveness Measures Suitable for Cost-Effectiveness | Main Effect of CGA and Geriatric Interventions | Cost-Effectiveness Propensity |
|--------------------|--------------|---------------|--------------------------------|-------------------------------------------------------|-----------------------------------------------|-----------------------------|
| Hempenius et al., 2013 [63] | 260 frail patients ≥ 75 years Mean age: 77 years Female: 77% Type of cancer: solid cancers (elective surgery) - 148 patients in the intervention group - randomisation stratified by cancer type - Frailty: GFI ≥ 3 | RCT | Geriatric liaison intervention to prevent PoD pre-operative CGA by a geriatric team, individual treatment plan, daily visits by a geriatric nurse during the hospital stay and advice on emerging medical problems. The intervention focused on best supportive care and the prevention of delirium. Control group: standard care (additional geriatric care was only provided at the request of the treating physician). | LoS, QoL | No significant difference between the groups in most aspects of the SF-36 scale to estimate QoL, although intervention group did not report significantly lower bodily pain at discharge than at admission compared with the usual-care group (OR: 0.49, 95% CI: 0.28–0.82). Neutral Positive |
| Lund et al., 2021 [67] | 142 frail patients ≥ 75 years Mean age: 75 years Female: 43% Type of cancer: stage II–IV CRC (receiving adjuvant (58%) or first-line palliative (42%) CT) - Frailty: G8 ≤ 3 - 71 patients in intervention group | RCT | CGA-based intervention: CGA at the start of CT, follow-up after 2 months or more frequently if needed. Interventions included medication changes (29%), nutritional therapy (51%), physiotherapy (39%), psychotherapy (39%), and DDI); final multidisciplinary medication review by the clinical pharmacist and a geriatrician team (recommendations to reduce ADE risk and ADE risk). A not significant trend was observed for a lower incidence of PoD between the intervention and usual-care group as well as for severity of PoD. This was a significant difference in term of return to preoperative living situation and care in favour of the intervention group, as opposed to the care dependency. | ADEs, CT completion | Grade 3–4 toxicity occurred in 20% of patients from the control arm and in 26% of patients from the CGA arm (p = 0.156), 20% in the intervention group and 38% in the control group discontinued CT due to toxicity (p = 0.175). More patients from the CGA arm completed the scheduled CT compared with controls (43% vs. 28%, p = 0.0344). Neutral Positive |
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| Choukroun et al., 2021 [85] | 51 frail outpatients ≥ 75 years Mean age: 81.1 years Female: 55% Type of cancer: not-hematologic solid cancers [breast (27%), CRC (16%), metastatic cancer (42%). - patients with G8 score ≤ 34 - median number of chronic comorbidities (including primary cancer) was 45 [high blood pressure (39%), dyslipidaemia (29%), chronic renal failure (22%), heart failure (20%) and type 2 diabetes (14%)]. | Prospect. observational study | Five-stage process (outpatient): preparation phase; face-to-face pharmaceutical consultation with the patient; CGA performed by an anesthesiologist and a geriatrician (geriatric tools, physical examination); pharmaceutical medication analysis (PIM, DDP, and DDI); final multidisciplinary medication review by the clinical pharmacist and a geriatrician team (recommendations to reduce DDP and optimise prescriptions). After the medication review, the proposals for prescription modification were sent to GPs and oncologists. | PIM, ADE risk PP | A significant decrease was observed in prevalence of PIM use and ADE risk. A not significant trend was observed for a lower number of medications. Positive |
**Table 3. Cont.**

| Authors                          | Participants                                      | Type of Study                                      | CGA and Geriatric Interventions                                                                 | Effectiveness Measures Suitable for Cost-Effectiveness | Main Effect of CGA and Geriatric Interventions | Cost-Effectiveness Propensity |
|----------------------------------|---------------------------------------------------|---------------------------------------------------|-------------------------------------------------------------------------------------------------|--------------------------------------------------------|-----------------------------------------------|----------------------------------|
| DuMontier et al., 2020 [60]      | 160 frail/prefrail patients [per-protocol intervention and control (n ≥ 148)] Median age: 85 years Female: 45% | RCT                                               | Frail and prefrail patients were randomised to standard oncologic care or standard care plus consultation with a geriatrician. Geriatricians provided individualised interventions, if indicated, for communication with patient’s primary care provider and utilised referral systems (e.g., psychiatry). Follow-up was encouraged, but not required. Most common interventions fell within the comorbidity/PP domain (92%); followed by nutrition (33%), function/ADLs (28%), cognition (15%) and depression/mood (19%). 40 patients in intervention group. 40 patients had at least one visit with a geriatrician. | Left ED visits Unplanned hospitalisations                                      | Consultation did not significantly reduce the incidence of ED visits, hospitalisations (6 months follow-up), or days in hospital. | Neutral |
| Li et al., 2020 [61]             | 605 patients Med. age: 72 years Female: 45%       | RCT                                               | Below-starting CT, both arms completed a baseline CGA and Fulmer SPICES assessment. In the intervention arm (GAIN), a geriatric-trained multidisciplinary team (oncologist, nurse practitioner, social worker, physical/occupational therapist, nutritionist, and pharmacist) acted on CGA results and implemented interventions. In the control arm (SOC), CGA results were sent to treating oncologists for consultation without any input from the multidisciplinary team. | Left ED visits Unplanned hospitalisations Hospital readmissions                | No significant differences were observed in ED visits, unplanned hospitalisations, average Left, unplanned hospital readmissions and ED between groups. | Neutral |
| Nadaraja et al., 2020 [64]       | 96 patients Med. age: 74 years Female: 45%        | RCT                                               | Control group: treatment decision based on oncologist’s clinical judgement. Intervention group if G8 ≤ 14: treatment decision based on G8 screening, followed by CGA, a multidisciplinary team conference and interventions. Intervention group if G8 > 14: treatment decision based on oncologist’s clinical judgement. | Treatment completion ADEs CT discontinuation                                     | Compared to SOC, GAIN arm experienced a significant 10.1% reduction in the incidence of grade 3–5 CT-related toxic effects. Reductions were observed for hematologic-only toxic effects (8.9% reduction) as well as non-hematologic-only toxic effects (9.2% reduction). No significant differences in dose modifications or discontinuations. | Positive Neutral |
| Nipp et al., 2020 [50]           | 62 patients Med. age: 72.3 years Female: 45%      | RCT                                               | Random assignment to usual care or intervention. Transdisciplinary intervention integrating geriatric and palliative care with oncology care (two visits with a geriatrician trained about geriatric-specific and palliative care issues and CGA). | QoL. Intervention patients presented less decrease in QoL decrement (FACT-G). | No impact on completion rate of planned oncologic treatment, but the intervention resulted in a borderline significant lower incidence of grade 3–4 toxicity. | Neutral Positive |
| Östrem et al., 2021 [71]         | 363 patients Med. age: 75 years Female: 45%       | RCT                                               | All patients received CGA at baseline performed by a multidisciplinary team with evaluation of patient health status. Intervention group received a tailored follow-up by a multidisciplinary team. Follow-up lasted 90 days, performed in-patient (either in the outpatient clinic or during hospitalisation), in the patient’s own home, or as phone calls. | Hospitalisations Completion of planned treatment ADEs Physical Performance | No significant impact on hospitalisation (4% of intervention vs. 9% of controls). No differences in ability to complete the treatment, ADEs or physical performance were found. | Neutral |
| Soo et al., 2020 [10,67]         | 130 patients Med. age: 75 years Female: 45%       | RCT                                               | Intervention group received integrated oncogeriatric care, CGA and management integrated with standard oncologic care. The group was oversampled by a geriatrician during oncological treatment, undergirding a CGA, standardised personalised interventions and recent health history, supports communication, encouragement of physical activity, management of comorbidities, medication reconciliation and advance care planning. Control group: managed by oncologist only, without input from geriatrician. | QoL. Unplanned hospital admissions ED visits                                    | Significant differences favouring the intervention group over the usual care group were seen in QoL—measured using EORTC QLQ-C30 and EORTC QLQ-ELD14 at 0, 12, 18 and 24 weeks—and unplanned hospital admissions (4% less) and ED visits (39% less). Intervention group presented significantly better ELFI than usual care group at all follow-ups. | Positive |

**Discussion on End of Life (EoL) goals**

Discussion on EoL goals: Consultation did improve the odds of having EoL goals of care discussions (OR: 3.12, 95% CI: 1.05–9.41).
Table 3. Cont.

| Authors | Participants | Type of Study | CGA and Geriatric Interventions | Effectiveness Measures Suitable for Cost-Effectiveness | Main Effect of CGA and Geriatric Interventions | Cost-Effectiveness Propensity |
|---------|--------------|---------------|--------------------------------|--------------------------------------------------------|-----------------------------------------------|-------------------------------|
| Ramsdale et al., 2018 [64] | 40 patients ≥70 years Mean and median age: 77 years Female: 45% Type of cancer: advanced solid cancer or lymphoma. Impairment in at least one geriatric domain other than PP. | Descriptive comparison study (subset of patients enrolled in RCT) | All patients received CGA at baseline, prior to starting antineoplastic therapy. In the intervention group, oncologists were given results of CGA. In the control group, they received no information. | Addressing PIM and PP | Physician-identified discussions were higher in intervention (72% vs. 48%; p = 0.006). More PP concerns brought up per patient (4.1 vs. 2.4; p = 0.07) and “addressed” in intervention compared with control (39% vs. 8%; p = 0.01). Medication management concerns were addressed more commonly in intervention (79% vs. 38%; p = 0.003). Supportive care medication concerns were more often addressed in control group (58% vs. 36%; p = 0.008). | Positive |
| Magnuson et al., 2018 [65] | 71 patients ≥70 years Mean age: 75 years Female: 44% Type of cancer: advanced (stages III or IV) solid tumour malignancy. | Prospective randomised pilot study | In intervention arm an algorithm was used to guide CGA management recommendations. The coordinator scored the GA and identified impairments, then summarised CGA impairments with management recommendations and delivered recommendations to the patient's primary oncologist within 1 week of assessment. At the 3-month follow-up timepoint, the primary oncologist reported whether these recommendations had been implemented. | Hospitalisations | Prevalence of hospitalisation did not differ between the two groups. | Neutral |
| Put et al., 2018 [75] and Sattar et al., 2019 [76] | 61 patients ≥70 years Mean age: 75 years Female: 36% Type of cancer: (stage I–IV) GI, GU, or breast cancer. | RCT | Intervention: CGA, interventions, first follow-up: 3 months after CGA, follow-up appointment if needed. Treating physician received the summary of findings and interventions that would be implemented by the clinical intervention team. Control group: usual care from the oncology team. | ADEs Treatment continuity | Incidence of grade 3–5 CT toxicity did not differ between the two groups. | Neutral |
| Carre et al., 2016 [66] | 484 patients ≥70 years Mean age: 77 years Female: 26% Type of cancer: advanced (stage IV) NSCLC (starting CT). | RCT | Intervention group: experimental CGA-based allocation of the same CT or BSC. Control group: standard strategy of treatment allocation (based on PS and age). | QoL, QoL-adjusted survival | Although QoL utility scores at baseline were not different between the arms, they were always higher (although not significantly) in the CGA arm than in the standard arm at each subsequent evaluation, with no evident negative impact of the 7% of patients who received exclusive BSC. The difference in QoL, utility scores was significant only at week 36 (p = 0.02). | Neutral |
| Kalis et al., 2015 [74] | 135 patients ≥70 years Mean age: 79 years Female: 45% Type of cancer: GI (35%), other (4%) (starting CT with or without ILT). | Prospective cohort comparison study | The intervention group underwent risk stratification using a patient-completed screening questionnaire and high-risk patients received geriatrician-delivered CGA. The observational control group received standard oncology care. | CT outcome ADEs CT management | Geriatrician-delivered CGA was associated with better outcomes. No significant trend for a lower grade 3+ toxicity rate in intervention (43.5% vs. 48.6% in the intervention group and 52.9% in the control). More participants in intervention completed treatment as planned (p = 0.006) and fewer required treatment modifications (p = 0.006). | Positive Positive |
| Bourdel-Marchasson et al., 2014 [66], Bagumte et al., 2021 [96] | 336 patients ≥70 years Mean age: 79 years Female: 44% Type of cancer: carcinoma (colon, stomach, pancreas and biliary tract, ovary, prostate, bladder, and lung) and lymphoma (treated with CT). Patients with at least KPS ≥50% and at risk of malnutrition (17 ≤ MNA ≤ 23). | RCT | The usual care received usual dietary recommendations. The intervention group received usual care and nutritional intervention. Counselling was based on face-to-face intervention and dietary advice cards and involved caregivers or relatives if possible. | Hospitalisation QoL ADEs | Analyses were performed on an ITT basis. The intervention was no beneficial for hospitalisation (intervention presented not significantly lower hospitalisations) and 1 and 2-year mortality (similar in both groups). Cancer cachexia anti-emabulums may explain this lack of effect. The intervention did not modify the HRQoL changes in comparison with routine care. | Neutral |

**Note:** The table continues with similar entries for other studies.
Table 3. Cont.

| Authors          | Participants                                                                 | Type of Study                                                                 | CGA and Geriatric Interventions                                                                 | Effectiveness Measures Suitable for Cost-Effectiveness | Main Effect of CGA and Geriatric Interventions | Cost-Effectiveness Propensity |
|------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------------|---------------------------------------------|----------------------------------|
| Rao et al., 2005 | 99 frail patients ≥65 years                                                  | Mean age: 74 years                                                            | Hospitalised on a medical or surgical ward, after stabilisation of acute illness, randomised to receive care in a geriatric inpatient unit/geriatric outpatient clinic/both/nether. In geriatric evaluation and management units (inpatient and outpatient geriatric units) core teams provided CEA and patient management. | LoS: Direct costs for care Qol.                       | Geriatric evaluation and management inpatient unit impacts the QoL (SF-36) in the management of bodily pain and mental and emotional health (no difference in SF-36 general scores between groups). These effects were achieved with no overall increase in hospitalisation or cost of care over the year of the study. No significant differences in LoS. No effect on mortality. | Neutral Positive Positive |

Abbreviations: ADLs: Activities of Daily Living; ADEs: Adverse Drug Events; AEs: Adverse Events; BSC: Best Supportive Care; CT: Chemotherapy; CGA: Comprehensive Geriatric Assessment; CRC: Colorectal cancer; DDI: Drug–Drug Interaction; DRP: Drug Related Problems; ED: Emergency Department; ELFI: Elderly Functional Index; EoL: End of Life; EQ-5D: EuroQoL-5 Dimension; EQ-5D-3L: 3-level version of EQ-5D; FACT-G: Functional Assessment of Cancer Therapy-General; GPs: General Practitioners; GU: genitourinary; HRQoL: Health-Related Quality of Life; IADLs: Instrumental Activities of Daily Living; ITT: Intention-To-Treat; KPS: Karnofsky PS; LoS: Length of Stay; MNA: Mini Nutritional Assessment; NSCLC: Non-Small-Cell Lung Cancer; OS: Overall Survival; PFS: Progression Free Survival; PIM: Potentially Inappropriate Medication; PP: polypharmacy; PS: Performance Status; RCT: Randomised Control Trial; RT: Radiotherapy; SF-36: Short Form-36 Health Survey; SPICES: Sleep disorders—Problems with eating/feeding–Incontinence–Confusion–Evidence of Falls–Skin Breakdown; TFFS: Treatment Failure-Free Survival; VES-13: Vulnerable Elders Survey. White rows: cost-sensitive measures (measures of patient health conditions leading to cost-increasing or cost-decreasing effects); grey rows: measures of effectiveness of CGA intervention (with the estimation of costs in two studies [81,86]).
The cancer site considered is colorectal cancer (CRC) in 10 studies [59,60,64,67,75,77–81]; CRC or esophagogastric cancer in 1 study [82]; gastrointestinal cancer (GI) in 1 study [72]; GI, gastro–urinary (GU) or breast cancer in another study [73]; GI or lung cancer in another study [70]; GI or other sites in another study [74]; GU, bladder, kidney or NSCLC in another study [69]; head and neck, lung, upper GI or CRC in another study [71]; NSCLC in another study [66]; prostate, lung, haematologic, GI, head/neck, bladder, renal and other sites in another study [86]; lymphoma, leukaemia or multiple myeloma in another study [65]; solid cancers in 4 studies [61,63,83,85]; solid cancers or lymphoma in another 4 studies [58,62,68,84] and different malignant neoplasms in another study [76].

The mean ages of the patients included in the identified studies varied between 72 and 83.7 years and the median ages ranged from 71 to 83 years.

The included studies published using data from Europe (12 studies [63,66–69,71,75,77–80,85]), followed by the USA (9 studies [28,61,62,70,72,83,84,86,90]), Hong Kong (2 studies [59,60]), the UK (2 studies [74,82]), Australia (1 study [58]), Canada (1 study [73]), Japan (1 study [64]) and Singapore (1 study [81]). Four articles were published between 2005 and 2014 [60,63,68,86], ten between 2015 and 2018 [59,64,66,73,74,77,79,82–84] and fifteen between 2019 and 2022 [28,58,61,62,67,69–72,75,76,78,80,81,85].

3.2. Studies Assessing the Effectiveness and Costs of CGA

Surgical and Medical Setting

Two studies out of the selected articles included measures of effectiveness of the CGA and estimated the direct costs of the intervention compared to the usual care. Even though the incremental cost-effectiveness ratio (ICER) was not performed, the cost-effectiveness of the interventions results were positive, since the CGA improved the outcomes at a lower cost when compared to the control group - by adopting the same approach already used by Eamer and colleagues [89] or improved the outcomes without raising the costs.

The first was a nonrandomised prospective before-and-after study conducted by Koh and colleagues that recruited 81 patients (≥70-years) with resectable colorectal cancer (CRC) scheduled for elective colectomy [81]. The geriatric intervention consisted of a standardised prehabilitation program (Programme for Enhanced Elderly Recovery at Sengkang General Hospital—PEERS). The program included the CGA, nutrition supplementation, resistance training, optimisation of the cardiac risk for operation and early evaluation of the patient home to ensure the residence was equipped to receive the patient after surgery. In addition to good results in the QoL for the PEERS group compared with the patients from the control arm (who were treated according to a standard-of-care approach), the average duration of hospitalisation in the PEERS group was 6.8 days shorter—after adjusting for surgical approach and complications—with an average USD 11,838.80 savings per patient [81].

The second, by Rao and co-authors, analysed from a health economic perspective a RCT that was conducted in 11 medical centres [86]. In this trial, 99 frail older patients (≥65 years)—who were hospitalised either in a medical or in surgical ward with a miscellaneous group of cancer diagnoses (solid and haematological malignancies)—were randomised to receive geriatric care or standard care. In the experimental arm, the CGA and the corresponding interventions were implemented by a physician, a nurse practitioner and a social worker. Although there was no effect of the CGA-driven interventions on the mortality and on overall QoL (36-Item Short-Form general health survey—SF-36 score), the inpatients who were treated according to a geriatric approach exhibited better mental health, less bodily pain and lower emotional limitation on the SF-36 scale than the usual inpatients at discharge. Overall, there was no significant difference between patients who received CGA-driven interventions vs. patients who were managed according to the standard of care in terms of the total hospital costs after one year (USD 47,300 vs. USD 45,500, respectively). Similarly, the total geriatric outpatient costs were also not significantly impacted by the intervention (USD 44,700 vs. USD 48,100 for patients managed through the CGA and patients managed according to the standard of care, respectively), as well as LoS. In this study, the costs that were taken into account included those of inpatient,
outpatient and long-term care provided by Veterans Affairs medical centres, whereas the costs of inpatient and outpatient care in other facilities, as well as care in private nursing homes, were not included [86].

3.3. Studies Reporting the Outcomes of CGA Interventions Other Than Treatment Toxicity

We identified 17 articles reporting the outcomes of interventions—often also used to rate the cost-effectiveness—in relation to CGA adoption in older cancer patients who were treated either in a surgical or in a medical setting.

3.3.1. Surgical Setting

Several studies of the CGA in older patients undergoing oncological surgery have been identified.

In the study conducted by Janssen and co-authors, a multimodal prehabilitation program—tailored to reduce the incidence of delirium and other adverse events (AEs) in older patients undergoing elective major abdominal surgery—had no effect on the Length of Stay (LoS), readmissions, unplanned ICU admissions, institutionalisation and postoperative complications but successfully reduced the incidences of delirium [80]. In the study conducted by Tarazona-Santabalbina, CGA-based interventions resulted in a lower incidence rate of delirium and other geriatric syndromes in the intervention group admitted for elective CRC surgery without a significant effect on readmissions, even if these patients had significantly poorer functional conditions, a higher prevalence of dementia and heart failure and a higher comorbidity burden at the baseline [75], contributing to serious complications that were more frequent in this group. A multicentre prospective RCT conducted by Hempenius and colleagues evaluated the effect of the CGA and CGA-driven interventions on the incidences of postoperative delirium (PoD) in older cancer patients (≥65 years) undergoing elective surgery for solid tumours [63]. The CGA intervention consisted of a preoperative geriatric consultation, an individual treatment plan targeted at the risk factors for delirium, daily visits by a geriatric nurse during the hospital stay and advice on how to manage the ensuing medical problems. The intervention failed in the main purpose, since there was no significant difference between the incidence of PoD in the intervention group and the usual care group. Similarly, there was no effect of the CGA on the postoperative complications, mortality or care dependency post-discharge. However, this study did find a positive effect of the CGA on bodily pain (SF-36 domain), with no increase in LoS [63].

In the retrospective study that was conducted by Indrakusuma and colleagues, the group undergoing a geriatric preoperative assessment (Dutch acronym: DOG)—consisting of a CGA and geriatric interventions—presented a higher prevalence of a history of delirium than the controls, but the tailored intervention resulted in a lower PoD for DOG patients compared to the controls [79]. Moreover, being at a higher risk than the controls, DOG patients had comparable postoperative general/surgical and medical complications, with no significantly shorter LoS and similar outcomes in mortality [79].

Ommundsen and colleagues showed that a preoperative geriatric assessment reduced the total number of grade I–V complications without increasing the LoS and reoperation rate in frail patients who received elective CRC surgery [64]. No statistically significant differences were found between the intervention group and the control group for reoperations or readmissions [64].

In the study by Shipway and colleagues, 132 patients underwent preoperative CGA and profited from geriatric medical care during hospitalisation [82]. Among the patients undergoing CGA, 36% of the patients who received a preoperative CGA were deemed noneligible for surgery. Overall, this study found that the CGA and the involvement of a geriatrician in patient care resulted in a LoS reduction of 3.1 days among the patients older than 60 years. The effect of the CGA and geriatric intervention was also found in patients (older than 60 years) who received emergency surgery, with a mean LoS reduction of 4.4 days. Conversely, in patients admitted for elective GI cancer surgery, no statistically
significant LoS reduction was observed, although the authors reported a trend towards a reduction with advancing age (particularly in patients ≥75 years who had a 5.2-day reduction in LoS) [82].

In the study of Ho and colleagues on older patients with colorectal cancer randomised to conventional surgical care or enhanced geriatric input, the median LoS was significantly shorter, and the postoperative complications were significantly lower in the intervention group when compared to the control [59].

Similarly, in a pilot study focused on enhanced geriatric input in the management of older patients undergoing CRC surgery conducted by Mak and co-authors, the patients who received geriatric input showed a shorter mean LoS and lower 30-day morbidity when compared with the controls [60].

In the cohort study carried out by Shahrokni and colleagues on older patients undergoing cancer-related surgical treatment, the intervention patients—receiving geriatric co-management—were older than those who received care managed by the surgery service only, but there were no differences in frailty measured by the Memorial Sloan Kettering Frailty Index (MSK-FI) [76]. Patients receiving co-management had longer operative times and longer LoS than the control group [76]. On the other hand, a higher proportion of patients in the geriatric co-management group received inpatient supportive care services, including physical therapy, occupational therapy, speech and swallow rehabilitation and nutrition services, and they had significantly lower 90-day postoperative mortality. The adverse surgical outcomes within 30 days of surgical treatment did not differ across the groups [76].

In the study conducted by Souwer and co-authors on older patients that underwent elective surgery for stage I–III CRC, the patients who benefited from a comprehensive multidisciplinary prehabilitation and rehabilitation care program showed a lower one-year overall mortality, a significant reduction in cardiac and severe complications and in the number of patients with a prolonged LoS [77].

In the cohort study carried out by van der Vlies and colleagues on frail older patients with CRC undergoing surgery resulted in comparable postoperative outcomes for frail patients compared to non-frail patients by means of a CGA intervention; they were even found at an increased risk for a worse OS [78].

In the RCT conducted by Nipp and co-authors on older patients with GI cancer undergoing surgery, the perioperative geriatric intervention (PERI-OP) did not have a significant impact on ICU use, hospital readmissions or complications. However, in the PP analysis, the subgroup who received PERI-OP as planned experienced significantly shorter postoperative hospital LoS [72].

3.3.2. Medical Setting

Concerning the studies of the CGA and GCA-driven interventions in older patients undergoing medical treatment, again, several examples of this approach are available in the literature, and we identified studies reporting measures sensitive to implications for the cost-effectiveness.

In the study conducted by Soo and co-authors evaluating older cancer patients who received systemic anticancer therapy, an integrated oncogeriatric approach led to improvements in health-related QoL, treatment discontinuation and a reduction in unplanned hospital admissions and ED visits [58].

DuMontier and colleagues found that, in prefrail and frail older patients with haematologic malignancies, an embedded geriatric consultation did not improve the acute care utilisation (not significantly reduced LoS, hospitalisations and ED visits), but it significantly increased the likelihood of having End-of-Life (EoL) goals of care discussed without an increase in acute care [65].

In the pilot RCT of a transdisciplinary intervention integrating geriatric and palliative care with oncology care carried out by Nipp and colleagues, consequently, in visits with a geriatrician and CGA intervention patients—with incurable GI or lung cancer—had
less decrease in QoL decrement, a reduced number of moderate/severe symptoms and improved confidence in communication compared to the usual care [70].

In the RCT of a tailored follow-up intervention on CGA in older frail patients with cancer conducted by Ørum and colleagues, even without a significant rate—a lower percentage of patients in the intervention group—were admitted to hospital during the study (47% vs. 55% of controls), while no differences in ability to complete the treatment, ADLs or the physical performance were found [71].

In the RCT carried out by Puts and co-authors [73], the CGA-based intervention on older cancer patients induced a slight benefit in QoL for the intervention patients, but in the secondary analysis conducted by Sattar and colleagues, the results of EQ-5D-3L at all timepoints presented no statistically significant differences between the two groups [88]. Sattar and colleagues also found no statistically significant differences between the intervention and control group in the number of ED and family physician visits, even with slightly lower rates in the intervention group [88].

3.4. Studies Reporting Outcomes of CGA Interventions: Treatment Toxicity and Other Complications

Medical Setting

Ten of the studies we identified investigated the impact of CGA in terms of the treatment toxicity, almost all resulting in a toxicity reduction, a good cost-sensitive outcome in representative cohorts of older cancer patients.

Li and colleagues conducted a RCT on older patients (≥65 years) with a solid malignant neoplasm (GI 33.4%, breast 22.5%, lung 16.0%, GU 15.0%, gynaecologic 8.9% and other cancer types 4.1%) who were starting a new chemotherapy regimen and completed a geriatric assessment [61]. Six hundred and five patients were enrolled in this trial. According to this study, a CGA-driven intervention implemented by a multidisciplinary team (oncologist, nurse practitioner, social worker, physical/occupation therapist, nutritionist and pharmacist who reviewed the CGA results and implemented interventions based on prespecified thresholds) significantly reduced the grade III/higher chemotherapy-emergent AEs. No significant differences were observed in the average LoS, unplanned readmissions and hospitalisations, ED visits and overall survival (OS), as well as in chemotherapy dose modifications or discontinuations [61].

Similarly, Mohile and colleagues performed a randomised controlled trial enrolling 718 patients (≥70 years) with an incurable solid cancer or lymphoma, at least one impaired CGA domain and who were starting a new treatment regimen [62]. The intervention that was evaluated was CGA-coupled with the geriatric assessment-guided management recommendations provided to the community oncologists. This trial found that the CGA and GCA-driven recommendations largely reduced the serious chemotherapy-emergent (grade III–V) ADEs and falls in patients with advanced cancer and aging-related conditions [62].

Choukroun and colleagues conducted a single-centre prospective study among 51 older outpatients with cancer (≥75 years), showing that CGA combined with a pharmacist consultation was effective at detecting and contrasting the use of potentially inappropriate medications (PIMs) [85].

Kalsi and colleagues evaluated the impact of CGA-driven interventions on chemotherapy toxicity and tolerance in older patients (≥70 years) with cancer undergoing chemotherapy [74]. The authors found geriatrician-led CGA interventions to be associated with improved chemotherapy tolerance with a reduced rate of (grade III/higher) toxicity (even if not significantly) after adjusting for age, comorbidity, metastatic disease and initial dose reductions [74].

In the study conducted by Corre and co-authors on older patients with advanced Non-Small-Cell Lung Cancer (NSCLC), treatment allocation based on the CGA slightly reduced the treatment toxicity [66].

In a RCT with 142 patients, Lund and colleagues showed that geriatric interventions increased the rate of completion of adjuvant chemotherapy and QoL, reducing the toxicity,
for frail older patients receiving chemotherapy for CRC [67]. Furthermore, more patients from the CGA arm completed the scheduled chemotherapy compared with the controls [67].

In the study conducted by Ramsdale and co-authors on 40 older patients with advanced solid cancer or lymphoma, more PP concerns were brought up and addressed in the intervention CGA group [84].

In the two-year RCT on nutritional advice conducted by Bourdel-Marchasson and colleagues on older patients treated with chemotherapy for carcinomas and lymphomas at risk of malnutrition, the diet counselling was efficient in increasing the dietary intake but had no beneficial effect on one-/two-year mortality; chemotherapy management (dosage, changes and arrest) and hospitalisations, even if the intervention group experienced non-significantly fewer hospitalisations [68]. There were more usual care patients with grade III to IV infections than in the intervention group, but the robustness analysis did not confirm the difference in the incidence of severe infections [68].

The results of the RCT carried on by Nadaraja and colleagues on 96 patients shown oncologic treatment allocation for frail older cancer patients based on G8 screening followed by CGA had no impact on treatment completion, OS or median progression-free survival (PFS) but resulted in a borderline significant lower incidence of grade III to IV toxicity in the intervention group compared with the control group [69].

In the pilot study conducted by Magnuson and co-authors on 71 older patients with advanced (stage III or IV) solid tumour malignancy, only 35.4% of the CGA recommendation was implemented by the primary oncologist, and the incidence of grade III–V chemotherapy toxicity did not differ between the intervention and control groups, as well as the prevalence of hospitalisation, dose reductions, dose delays and early treatment discontinuation [83].

The studies identified are heterogenous for what concerns the setting, the sample size, the characteristics of the patients (for example, different types of malignancies and presenting with frailty or geriatric syndromes) and the aim of the CGA [91].

The parameters specifically adopted to rate the cost-effectiveness retrieved in these studies are scarce; only two studies reported effectiveness measures and costs, allowing to compare the outcomes and change in costs [81,86]. These studies focused on resource utilisation, institutional care costs, costs for readmissions and costs of direct health service uses.

Twenty-three studies included the measures of effectiveness of CGA interventions in terms of clinical outcomes and quality of life, such as Quality-Adjusted Life Years (QALYs) or proxy outcomes, the most recurrent being hospital readmissions and re-operations, LoS, unplanned hospitalisations and ICU or ED admissions (grey rows in Tables 2 and 3) [28,59–61,63,64,66–68,70–73,75,77–83,86,90]. All these measures have been frequently adopted in the literature to rate the cost-effectiveness—in particular, LoS as a proxy measure for resource use [92,93], here interpreted as cost-driven or cost-saving measures, a proxy for the propensity of cost-effectiveness of the specific CGA intervention, since the studies lack of actual cost estimations, with the exemption of the studies by Rao and colleagues [86] and Koh and co-authors [81].

Furthermore, almost all studies have reported cost-sensitive measures—measures of patient health conditions implying cost-increasing or cost-decreasing effects, even if not estimated in terms of costs, such as postoperative complications, toxicity, PP, PIM, therapy completion, CT tolerability and falls (white rows in Tables 2 and 3). In almost all studies, at least one dimension was positively impacted by the adoption of CGA in older patients. The LoS and severity of ADEs are the most reported measures, with a plausible good cost–benefit rate in the majority of studies (Table 4).
Table 4. Most recurrent reported measures for effectiveness of CGA interventions.

| Measures | Evidence in Identified Studies |
|----------|--------------------------------|
| LoS      |                                |
| Nipp et al., 2022 [72] RCT (96 patients) | positive |
| Koh et al., 2021 [61] Before-and-after (81 patients) | neutral |
| DeMontier et al., 2020 [65] RCT (160 patients) | neutral |
| Li et al., 2020 [61] RCT (669 patients) | neutral |
| Sharbafi et al., 2020 [74] Retrospective (1882 patients) | neutral * |
| van der Vlas et al., 2020 [79] Retrospective (435 patients) | neutral |
| Jansen et al., 2019 [80] Before-and-after (1852 patients) | neutral |
| Tarazona-Santabalbina et al., 2019 [75] Retrospective (1892 patients) | neutral |
| positive positive neutral neutral negative neutral |                |
| Ommundsen et al., 2018 [64] RCT (122 patients) | neutral |
| Shipway et al., 2018 [62] Before-and-after (602 patients) | positive |
| Sessier et al., 2018 [73] Retrospective (96 patients) | neutral |
| Ho et al., 2017 [69] RCT (74 patients) | neutral |
| Indrakusuma et al., 2015 [70] Retrospective cohort study (130 patients) | positive |
| Mak et al., 2014 [60] RCT (74 patients) | neutral |
| Hempenius et al., 2013 [61] RCT (209 patients) | neutral |
| Rao et al.2005 [74] Secondary analysis (of RCT) (99 patients) | neutral |
| neutral positive positive positive positive neutral positive neutral |                |
| ADEs     |                                |
| Lund et al., 2021 [67] RCT (412 patients) | positive |
| Mohile et al., 2021 [62] RCT (731 patients) | positive |
| Choukroun et al., 2021 [63] Prospective (51 patients) | positive |
| Li et al., 2020 [61] RCT (669 patients) | neutral |
| Nadaraja et al., 2020 [69] RCT (96 patients) | neutral |
| Magnuson et al., 2018 [63] RCT (75 patients) | neutral |
| Curren et al., 2016 [64] RCT (692 patients) | neutral |
| Kahl et al., 2015 [64] RCT (135 patients) | neutral |
| Bourdel-Marchasson et al., 2014 [64] RCT (338 patients) | neutral |
| neutral positive neutral |                |

* Frail patients in the intervention group. Abbreviations: ADEs: Adverse Drug Events; LoS: Length of Stay; RCT: Randomised Control Trial.
4. Discussion

The limited number of studies retrieved in our review indicates the lack of research on the topic of cost-effectiveness implications in CGA interventions. This result is consistent with the scarcity of combined medical and economic evaluations of older patients’ care [94].

Despite the limited number and the large heterogeneity among the studies identified in our review, the overall evidence rate is in favour of a measurable benefit from the CGA in the management of older patients with cancer in terms of reduced LoS (or at least stable LoS) and treatment toxicity and in improved clinical outcomes both in the medical and surgical settings (see Tables 2 and 3).

These results contribute to the evidence for an “investment effect” of the CGA. This concept—originated in the 1980s—was recalled by Wieland in his review of the CGA cost-effectiveness, meaning the investment of resources in the patient, not in the entire cohort of patients, providing more appropriate services wherein the costs of more appropriate care are offset by the less use of expensive institutional services [41].

Several studies showed that the CGA improves the profiling of older patients and, as a result, the tailoring of treatments. A validated prediction model designed by Hurria and colleagues was proven to independently predict the risk of treatment toxicity [9,95], as well as Extermann and colleagues, who elaborated and validated the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH), allowing for toxicity risk-stratification across a wide range of chemotherapies [96]. Ultimately, the CGA could well also be cost-effective thanks to its ability to select more patients for the best supportive care (instead of active treatment), preventing patients from experiencing severe toxicity and a rapidly worsening quality of life but also saving the costs of expensive anticancer medications and of the hospitalisations and treatments required for chemotherapy AEs (i.e., antibiotics, recombinant hematopoietic growth factors, etc.) [66]. Orienting the therapeutic choices, CGA instruments can also offer a valid contribution in avoiding overtreatments that lead to a worsening of the quality of life and avoidable costs. In Table 5, we report the costs of neutropenia, thrombocytopenia and anaemia, the most frequent haematological complications of cancer treatments [97].

Table 5. Costs for hospitalisation and adverse events treatments.

| Country                   | Cost Estimates                                                                 |
|---------------------------|-------------------------------------------------------------------------------|
| United States [98]        | Median cost per day of inpatient visits for older patients with cancer: USD 2108—USD 3468 |
| United States [97]        | Direct cost of neutropenia per episode: USD 1893 (outpatient)/USD 2893 (inpatient)—USD 38,583 (febrile neutropenia hospitalisation) |
| UK and Europe [97]        | Direct cost of neutropenia per episode: USD 300 (non-febrile cases)—USD 32,395 (older breast cancer patients) |
| United States [97]        | Direct cost of thrombocytopenia per cycle/episode: USD 1035—USD 5328          |
| Europe [97]               | Direct cost of thrombocytopenia per cycle/episode: USD 790—USD 2523           |
| United States [97]        | Direct cost attributable of anaemia per year: USD 18,418—USD 69,478          |
| Canada and Europe [97]    | Total cost of anaemia per episode: USD 124—USD 2704                          |
| United States and Europe [99] | Average total cost per ICU/day: estimated at EUR 1200                        |
| Europe [99]               | Direct costs per sepsis patient (ICU): estimates of EUR 23,000—EUR 29,000.   |
| United States [99]        | Direct costs per sepsis patient (ICU): estimates of EUR 34,000               |
| United States [100]       | Costs for severe sepsis cancer hospitalisation: USD 27,400                    |
|                           | Costs for surgical cancer severe sepsis hospitalisation: USD 48,000           |
|                           | Costs for medical cancer severe sepsis hospitalisation: USD 18,200            |
|                           | Costs for non-severe sepsis cancer hospitalisation: USD 8,700                 |
| United States [101]       | Healthcare costs per delirious patient per year: USD 60,516—USD 64,421       |
Seven of the identified studies in our review showed a positive effect of the CGA on treatment tolerance and toxicity. In the study conducted by Kalsi and colleagues [74], a geriatrician-delivered CGA was associated with better outcomes for older people undergoing chemotherapy (higher frequency of treatment completion and lower frequency in treatment modifications), with a lower chemotherapy toxicity, even if not significantly. Mohile and co-authors [62], Choukroun and colleagues [85], Lund and co-authors [67], Li and co-authors [61], Nadaraja and colleagues [69] and Corre and co-authors [66] showed that the adoption of the CGA resulted in a lower treatment toxicity. These results imply large cost reductions in the face of improvements in clinical outcomes, suggesting that interventions are cost-effective.

Table 5 shows an estimate of the costs that hospitals incur in for the management of geriatric cancer patients, including ADEs (these costs are extrapolated from the literature).

Among the evidence collected in our review, the CGA also appears to be an effective approach to symptom management and in assisting the management of pain and the emotional and mental health in older cancer patients, resulting in sustained improvement in the quality of life with no increase in costs [63,86]. These results were obtained in a medical [86] and in a surgical setting [63]. In the study conducted in a medical setting [86], the overall costs for institutional care were calculated and resulted equally in between the intervention and control group. In the other study [63], the LoS was similar between the intervention and control group, suggesting that a positive effect in the quality-of-life outcomes was obtained in a cost-effective way.

This review had some limitations. The studies included frequently enrolled small numbers of patients with different study designs. RCTs are present [58,59,61–73], together with cohort studies [44,102], before-and-after studies [80–82], pilot studies [60,83], a descriptive comparison study [84], a prospective observational study [85] and a secondary analysis study (of RCT) [86]. In addition, the CGA and CGA-driven interventions are not standardised. The cancer sites and outcomes reported are heterogenous, as well as genre balance and mean age of the study populations, even if the focus of all the studies was on older patients. Furthermore, it is difficult to analytically assess the cost-effectiveness of interventions because of the lack of studies implementing full economic evaluations and the heterogeneity among the studies in terms of the outcomes and cost estimations. For this reason, our analysis shifted only for qualitative arguments.

Currently, the lack of research on the CGA in oncology and on the cost-effectiveness of CGA-driven interventions does not allow to evaluate the cost-effectiveness of all the clinical benefits the CGA provides, including, for instance, the reduced risk of the institutionalisation of cancer patients [44,102] and the improved appropriateness of care [103].

More research is needed on the cost-effectiveness of the CGA in geriatric oncology, as well as the adoption of standard measures for this purpose.

Moreover, to enable the adoption of CGA in oncology, a solid interprofessional collaboration and a careful choice of the right instruments are crucial [104,105]. McKenzie and colleagues proposed to leverage information technologies to reduce the CGA implementation costs and to enable implementation of the CGA without the need for a dedicated geriatric oncology team/service [35]. This can be a valid choice, but the role of geriatricians in interpreting the CGA and in prescribing the resulting intervention remains crucial [106]. To pursue the minimisation of the costs, a good approach is integrating the geriatrician-led services required into existing structures (e.g., internal liaison and geriatric day clinic), promoting inter-speciality cross-fertilisation [35].

5. Conclusions

Our review highlights the lack of research on the topic of the cost-effectiveness implications of CGA interventions. Altogether, the results of our review support an “investment effect” of CGA in oncology. Despite overall not being tailored to rate the cost-effectiveness by design, the available evidence suggests that the CGA provides measurable benefits in older cancer patients with cost-savings effects, such as reductions in LoS—or stability of
LoS in the face of improved clinical outcomes—and decrease in ADEs, leaning toward a positive cost-effectiveness of the CGA in geriatric oncology. However, more research employing full economic evaluations is needed to confirm this evidence. Further, dedicated studies are needed to optimise the CGA approach for different settings and to tailor CGA instruments to the available human and professional resources.

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