Universiteit
Leiden
The Netherlands

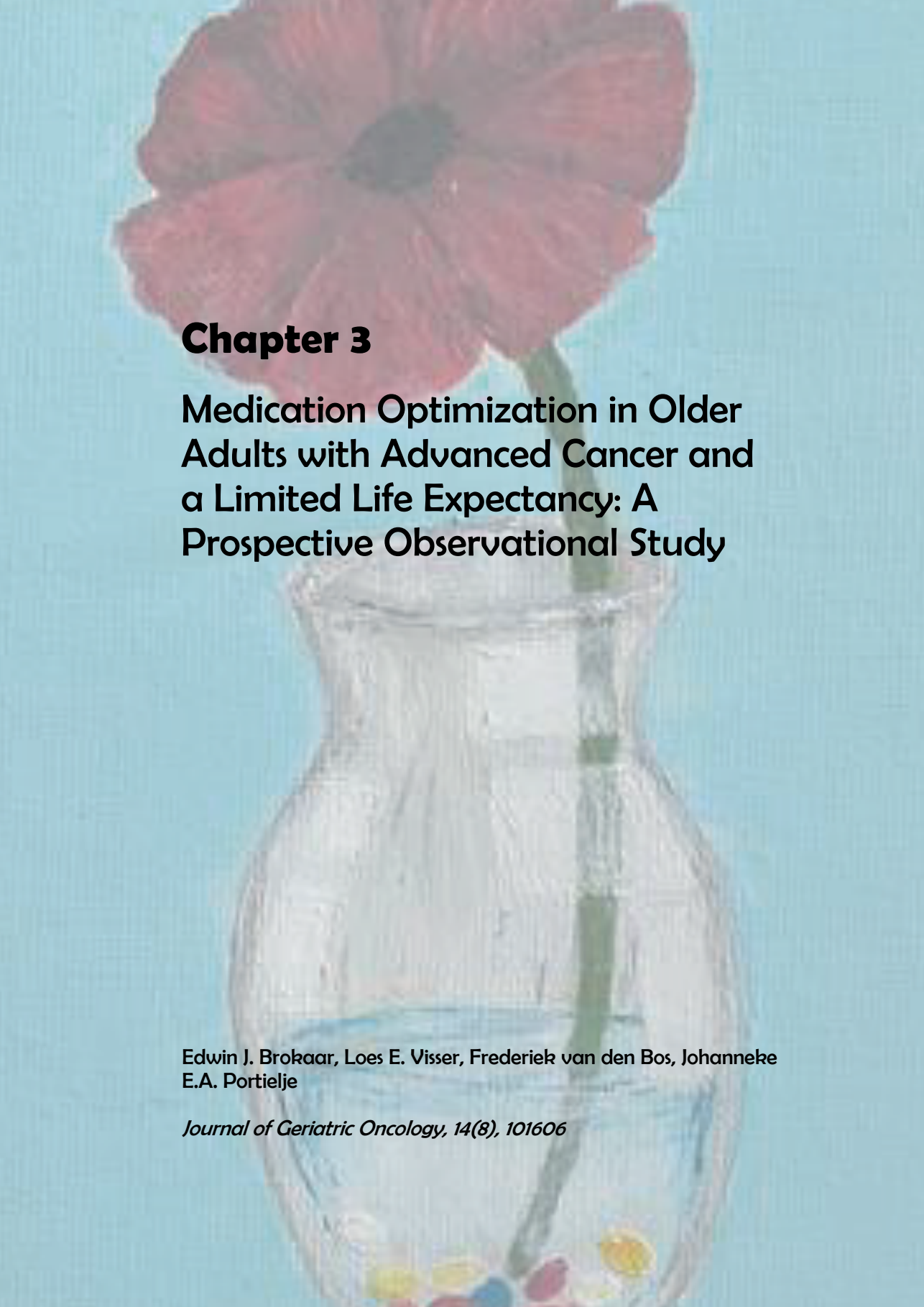
# Medication optimisation in older adults with cancer

Brokaar, E.J.

**Citation**
Brokaar, E. J. (2026, September 1). *Medication optimisation in older adults with cancer*. Retrieved from https://hdl.handle.net/1887/4308795

| | |
|---|---|
| Version: | Publisher's Version |
| License: | Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden |
| Downloaded from: | https://hdl.handle.net/1887/4308795 |

**Note:** To cite this publication please use the final published version (if applicable).



# Chapter 3

## Medication Optimization in Older Adults with Advanced Cancer and a Limited Life Expectancy: A Prospective Observational Study

Edwin J. Brokaar, Loes E. Visser, Frederiek van den Bos, Johanneke E.A. Portielje

*Journal of Geriatric Oncology, 14(8), 101606*

## Abstract

*Introduction*

Polypharmacy is common in older adults with cancer and is associated with drug related problems (DRPs) and potentially inappropriate medication (PIM). We introduced a medication optimization care pathway for older adults with advanced cancer and a limited life expectancy and studied the prevalence of DRPs and PIMs as well as the adherence to medication-related recommendations and the patient satisfaction.

*Materials and Methods*

A medication review was performed in patients aged ≥65 years with polypharmacy and a life expectancy of <24 months. Recommendations on adjustments of medication were discussed in a multidisciplinary team including a pharmacist, an oncologist, and a geriatrician. Implementation of the recommendations was left to the discretion of the oncologist. Four weeks after the implementation, the patient filled a questionnaire to assess satisfaction.

*Results*

One hundred twenty patients were included. The mean age was 75 years and 39% were female. A mean of 12 medications was used. The median number of DRP was 6.0 per patient and median number of PIMs was 3.0 per patient. Overtreatment accounted for 26% of DRP and the most frequently involved drug classes were antihypertensive medication (22%), non-opioid analgesics (22%), and antilipemics (12%). The multidisciplinary team accepted 78% of the recommendations of the pharmacist and the oncologist implemented 54% of the recommendations. Overall, patients were satisfied or very satisfied with the intervention.

*Discussion*

DRPs and PIMs are highly prevalent in this population and can be reduced by a multidisciplinary medication optimization intervention. Patients appreciate the medication optimization intervention and are satisfied with the intervention.

## Introduction

In the U.S, over 50% of newly diagnosed cancers and about 70% of cancer-related deaths are in patients of ≥ 65 years [1] and over 90% of these patients have one or more comorbidities [2]. As a result, polypharmacy is highly prevalent in older adults with cancer [3]. Medication deprescription is a fundamental ingredient of end-of-life care, but still uncommon for patients with advanced cancer during active cancer therapy. However, a higher drug burden is associated with the occurrence of drug related problems (DRPs), a higher probability of potentially inappropriate medications (PIMs), and lower quality of life [4, 5]. Patients with advanced cancer usually have a limited life expectancy and the focus of medical treatment may shift towards quality of life and the treatment of symptoms rather than the prevention of future risks, such as cardiovascular events.

Several studies have shown that polypharmacy and PIM use frequently occur in older patients with cancer. Up to 81% of patients with cancer use medications for previously diagnosed comorbidities [6] and PIM use ranges from 16% to 52% [7-10]. Our review of the literature on deprescribing in older adults with cancer and a limited life expectancy showed that 34 to 47% of all medications in various groups of older patients could safely be discontinued [11-14]. The medication groups with the highest success rates of discontinuation across these studies are antihypertensive medications, statins, gastric acid suppressants, bisphosphonates, and oral antidiabetic medication. As older patients with cancer are expected to have a shorter life expectancy than the majority of the patients in these studies, reducing PIM use should be possible as well in older adults with cancer.

Many studies use one or more explicit lists to identify PIMs, such as the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults or the Screening Tool of Older People's Prescriptions (STOPP criteria) [15, 16]. Those tools were developed for the general older population and not for patients with cancer. Many DRPs (36-51%) are not identified simply by explicit criteria in older adults with cancer [17, 18], but require information on the individual patients' experience with medication. Therefore, a medication-related intervention that targets the needs of patients should focus on both the reduction of inappropriate medications and of DRPs in the wider sense by incorporating information derived from the patient.

This prospective observational study describes the results of a consecutive cohort of older adults with advanced cancer and a limited life expectancy who participated in a newly introduced medication optimization care pathway. The care pathway consisted of a pharmacist-led interview to identify DRPs and PIMs and a subsequent multidisciplinary team meeting to decide upon advice concerning the medication for the treating oncologist and patient to discuss. We studied the prevalence of DRPs and PIMs in these patients, as well as the adherence to the recommendations about the medications involved in the DRPs and PIMs. We also tested whether various patient characteristics were associated with the occurrence of DRPs and PIMs and inquired after the patient satisfaction with the medication optimization intervention.

## Materials and Methods

*Setting and Population*

The medication optimization intervention was introduced as an improvement to the standard care for older adults with cancer in the Haga Teaching Hospital and was offered to all patients who met the following criteria:

- a diagnosis of cancer with an estimated life expectancy of < 24 months
- starting a new systemic, palliative cancer treatment
- age ≥ 65 years
- ≥ 5 systemically administered medications for other purposes than treating cancer

Life expectancy was estimated based on the median survival for type and stage of cancer or was based on the expectation of the oncologist. The treating oncologist consulted the pharmacist to execute the medication optimization intervention for individual patients. At the end of interview with the pharmacist, patients were asked for consent to use their data for the analysis described in this paper. If a patient did not provide written consent, the medication optimization intervention was performed as usual. The Medical Ethical Committee (METC-ZWH) concluded that the Medical Research Involving Human Subjects Act (WMO) did not apply and no ethics approval was required. This study was performed after the subsequent approval of the board of the Haga Teaching Hospital. Participants were recruited from April 2016 until January 2021 and follow-up ended in April 2021, three months after the last medication optimization intervention.

*Intervention*

The medication optimization intervention started with a semi-structured interview with a trained pharmacist. During the interview, the pharmacist addressed overall patient preferences with respect to their medication use, discussed all medications with a specific focus on possible adverse drug reactions, adherence, and practical issues. Correct use of the medications was verified and adjusted if necessary. Patients were also offered the opportunity to ask questions about their medications or treatments. The information obtained in the interview was combined with the electronic medical record to perform a comprehensive pharmaceutical analysis and identify DRPs and PIMs. PIMs were identified using the STOPP-criteria [16] supplemented with the judgment of the pharmacist. Recommendations of the pharmacist on discontinuation or adjustment of the medications involved in the DRPs and PIMs were discussed in a multidisciplinary team meeting that consisted of a pharmacist, an oncologist, a geriatrician, and specialized nurses until consensus was reached. The consensus recommendation was forwarded to the oncologist and discontinuation or adaptation of DRPs and PIMs was left to the discretion of this oncologist.

Four weeks after the visit to their oncologists in which the recommendations were discussed with the patient, the patients received a questionnaire on their satisfaction about various aspects of the medication optimization intervention. Answers were given using a five-point Likert scale ranging from ‘very dissatisfied’ to ‘very satisfied’. Prior to sending the patient satisfaction questionnaire, the investigators verified with the oncologist or specialized oncology nurse whether sending the questionnaire was still appropriate. If patients already had died or were approaching death, the questionnaire was not sent. The questionnaire is provided in Supplementary I.

*Outcomes*

The primary outcome was the number of DRPs per patient at the time of the interview. DRPs were classified according to a modified version of Cipolle et al. [19].The two categories *dosage too high* and *dosage too low* were merged into one category, *wrong dosage*. The category *unnecessary drug therapy* was specified and divided into two categories: *no indication* and *overtreatment*. Furthermore, four categories were added: *drug-drug-interaction*, *contraindication*, *duplicate medication*, and *other*. Table 1 displays the definitions of the various categories of DRPs.

Secondary outcomes were the number of PIMs per patient and the proportion of PIMs compared to the number of medications of a patient. Medications were considered potentially inappropriate if the pharmacist considered the medication potentially unnecessary, had no additional value, or when a safer, more effective, or better-tolerated option was available. Other secondary outcomes were the proportion of recommendations from the pharmacist that was accepted by the multidisciplinary team and the proportion of recommendations from the multidisciplinary team that was implemented by the oncologist. Furthermore, associations between age, sex, World Health Organization performance status (WHO-PS), Geriatric-8 (G8) [20], Adult Comorbidity Evaluation-27 (ACE-27) [21], and the number of DRPs and the number of PIMs were studied, as well as the satisfaction of the patients regarding the medication optimization intervention.

Adherence to the recommendations across the process of the medication optimization intervention was evaluated for every DRP as to whether the pharmacist's recommendation was accepted by the multidisciplinary team, and subsequently whether the oncologists accepted and implemented the recommendation of the multidisciplinary team. Acceptance and implementation were scored as yes, no, or not applicable (n/a). Not applicable was applied for DRPs that were resolved before they reached the following step in the medication optimization intervention process, such as patient instructions that were given during the interview. Unknown was applied if acceptance of a recommendation could not be retrieved, for example, recommendations on over-the-counter preparations.

The number of medications was based on the number of pharmacologically active substances used either chronically or 'as needed' for purposes other than treating cancer. Endocrine therapy in hormone sensitive cancers was considered cancer treatment and not included in the number of medications per patient, whereas supportive treatment like anti-emetics or treatment of bone metastases (bisphosphonates, denosumab) were included. The same medication applied in different preparations was calculated as one medication, for example, a slow-release opioid analgesic combined with the same medication as needed. For fixed medication combinations, the separate active ingredients were counted. Locally applied medications were not counted (eye and ear preparations, topical preparations), but inhaled medications were considered systemically applied medications.

**Table 1. Classification of Drug Related Problems**

| Category | Definition |
|---|---|
| Prescribing omission | a medication that should be prescribed is missing |
| No indication | the medication does not have a current indication |
| Overtreatment | there is an indication for the medication, but treatment goals are kept too strict with respect to the prognosis |
| Wrong drug | a more appropriate medication is available |
| Wrong dosage | dose should be increased or decreased |
| Drug-drug interaction | clinically relevant drug-drug interaction |
| Contraindication | clinically relevant contraindication for the use of the medication |
| Duplicate medication | two medications of the same pharmacological class that should not be prescribed together |
| (Possible) ADR | a perceived or actual adverse drug reaction |
| Noncompliance | any issue that hinders an effective administration of the medication |
| Drug ineffective | medication does not have a sufficient effect despite adequate dosing |
| Other | any issue not captured by one of the other definitions |

Abbreviations: ADR – Adverse drug reaction

*Cofactors*

Prior to the interview, patients were screened for frailty using the G8 screening tool by the specialized oncology nurse. WHO-PS was established by the oncologist, and the ACE-27 was calculated by the researchers using information from the patient's medical file. ACE-27 is a tool to grade the severity of diseases and conditions in cancer patients into an overall comorbidity score of grade 1 (mild), grade 2 (moderate), or grade 3 (severe) and was used for analytical purposes in this study only [21].

*Analysis*

Descriptive statistics were used to describe patient characteristics and outcomes as DRPs, PIMs, and the patient satisfaction questionnaire. Linear regression was used to test for associations between continuous variables (age, number of medications, and G8) and the number of DRPs or PIMs. G8 was also recoded into a dichotomous variable of ≤14 or >14, representing frail and non-frail patients, respectively. Sex and dichotomized G8 were tested using the Mann-Whitney U test for an association with the number of DRPs and the number of PIMs, and WHO PS and ACE-27 were tested using the Kruskal Wallis test.

## Results

A total of 268 patients met the inclusion criteria, of which 120 were included in this study. Figure 1 shows the reasons for exclusion. Patient characteristics are displayed in Table 2. The mean age was 74.9 ± 6.2 years and 39% were female. On average, patients used 11.9 ± 3.7 medications at the time of the interview. Most patients suffered from gastrointestinal cancer (22%), prostate cancer (31%), or lung cancer (22%). Nearly all patients had active comorbidities with an ACE-27 score of 1, 2, or 3 (43%, 34%, and 20%, respectively). Ninety-two percent of the patients had hypertension or cardiovascular diseases, respiratory diseases

(16%), endocrine diseases (28%), and neurological diseases (23%). At the end of the follow-up, 94 patients had died. Median time until death after the multidisciplinary team meeting was 263 days (interquartile range [IQR] 127-476).

The median number of DRPs was 6.0 (IQR 4.0-7.8) per patient. Overtreatment accounted for 26% of the DRPs and 16% of the DPRs were for a medication without an actual indication. Of the various medication classes, most DRPs were caused by antihypertensive medication (22%), non-opioid analgesics (22%), antilipemics (12%), and gastric acid suppression (11%). The median number of PIMs was 3.0 (IQR 2.0-5.0) per patient, 29.2 ± 15.1% of all the patient's medications were a PIM, and PIMs were involved in 68% of the DRPs.

The multidisciplinary team agreed on 78% of the pharmacist's recommendations on DRPs and rejected 13%. Nine percent of the pharmacist's recommendations had already been resolved with the patient.

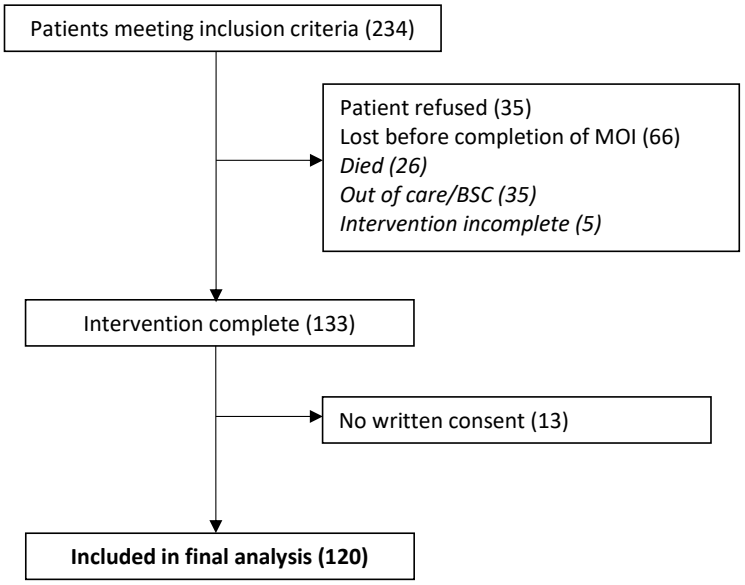
Of the recommendations that the multidisciplinary team subsequently made to the treating oncologist, 54% were actioned, 31% were not, and 15% were not applicable or unknown. As for the PIMs, the percentages were higher with 87% of the recommendations being agreed upon by the multidisciplinary team and 57% subsequently being effectuated by the oncologist.

Results of the medication optimization intervention are shown in Table 3 and Table 4. Possible adverse drug reactions accounted for 12% of DRPs and in 79% of these the suspected medication was a PIM. Antihypertensives were the medications that accounted for 22% of all DRPs. Other medication classes that generated many DRPs were antilipemics (12%) and gastric acid suppression (11%). Within the medication classes of antilipemics, antihypertensives, osteoporosis medication, oral antidiabetics, oral steroids, and urogenital medications, 80% or more of the DRPs were caused by a PIM.

The number of medications was positively associated with both the number of DRPs and of PIMs ($p<0.001$), but age, sex, WHO-PS, ACE-27, and G8 were not.

A total of 101 surveys were sent of which 61 were returned, for a response rate of 60%. Overall, patients were satisfied or very satisfied with the various aspects of the medication optimization intervention. The results of the patient satisfaction survey are displayed in Figure 2. Sixty-two percent of the respondents indicated that the medication optimization intervention resulted in a change in their medication. If a change in medication occurred, 71% were not concerned, 5% were concerned, 8% were a little concerned, and 16% did not respond to this question.

**Figure 1. Recruitment and exclusion**




Abbreviations: MOI – Medication Optimization Intervention; BSC – Best Supportive Care

**Table 2. Patient characteristics**

| | N = 120 |
|---|---|
| **Age, years (mean (SD))** | 74.9 (6.2) |
| **Sex (n (%))** | |
| Male | 73 (60.8) |
| Female | 47 (39.2) |
| **Number of medications* (mean (SD))** | 11.9 (3.7) |
| **BMI (mean (SD))** | 26.3 (4.4) |
| **Type of cancer (n (%))** | |
| Gastro-intestinal | 26 (21.7) |
| Breast | 14 (11.7) |
| Prostate | 37 (30.8) |
| Lung | 26 (21.7) |
| Female reproductive tract | 4 (3.3) |
| Kidney | 5 (4.2) |
| Other | 8 (6.7) |
| **ECOG PS (n (%))** | |
| 0 | 43 (35.8) |
| 1 | 43 (35.8) |
| 2 | 10 (8.3) |
| 3 | 4 (3.3) |
| Unknown | 20 (16.7) |
| **G8 (n (%))** | |
| >14 | 20 (16.7) |
| ≤14 | 43 (35.8) |
| Unknown | 57 (47.5) |
| **ACE-27 (n (%))** | |
| 0 | 4 (3.3) |
| 1 | 51 (42.5) |
| 2 | 41 (34.2) |
| **3** | **24 (20.0)** |

Abbreviations: ECOG PS – Eastern Cooperative Oncology Group Performance Status; ACE – Adult Comorbidity Evaluation; BMI – Body Mass Index

*systemically administered medications for other purposes than treating cancer

**Table 3. Frequency of DRP**

| Category of DRP | Total (N (%)) | Of which labelled PIM (N (%*)) |
|---|---|---|
| **Total** | **725 (100)** | **490 (67.6)** |
| Prescribing omission | 38 (5.2) | - |
| No indication | 114 (15.7) | 114 (100) |
| Overtreatment | 188 (25.9) | 188 (100) |
| Wrong drug | 26 (3.6) | 21 (80.8) |
| Wrong dosage | 33 (4.6) | 8 (24.2) |
| Drug-drug interaction | 58 (8.0) | 34 (58.6) |
| Contraindication | 5 (0.7) | 5 (100) |
| Duplicate medication | 5 (0.7) | 5 (100) |
| (Possible) ADR | 88 (12.1) | 69 (78.4) |
| Noncompliance | 36 (5.0) | 4 (11.1) |
| Drug ineffective | 32 (4.4) | 11 (34.4) |
| Other | 102 (14.1) | 31 (30.4) |

Abbreviations: DRP – Drug Related Problem; PIM – Potentially Inappropriate Medication; ADR – Adverse drug reaction

*percentage within category

**Figure 2. Patient satisfaction**

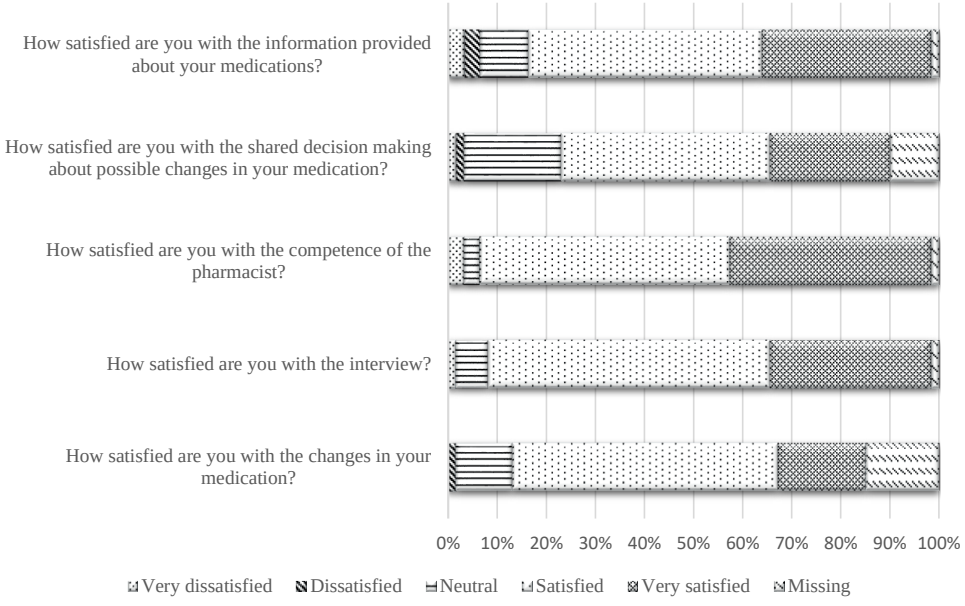


**Table 4. Acceptance of recommendations per drug class**

| Drug class | Total (N (%)) | PIM (N (%*)) | Recommendation pharmacist accepted by MDT (N (%*)) | | | Recommendation implemented[#] (N (%*)) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | **Yes** | **No** | **n/a** | **Yes** | **No** | **n/a** | **Unknown** |
| **Total** | **725 (100)** | **490 (67.6)** | **562 (77.5)** | **95 (13.1)** | **68 (9.4)** | **387 (53.4)** | **225 (31.0)** | **82 (11.3)** | **31 (4.3)** |
| Antiplatelets/anticoagulants | 37 (5.1) | 21 (67.7) | 30 (81.1) | 4 (10.8) | 3 (8.1) | 26 (70.3) | 7 (18.9) | 2 (5.4) | 2 (5.4) |
| Antilipemics | 88 (12.1) | 84 (95.5) | 84 (95.5) | 1 (1.1) | 3 (3.4) | 62 (70.5) | 23 (26.1) | 3 (3.4) | - |
| Antihypertensives | 161 (22.2) | 137 (85.1) | 129 (80.1) | 27 (16.8) | 5 (3.1) | 88 (54.7) | 65 (40.4) | 8 (5.0) | - |
| Osteoporosis medications | 57 (7.9) | 47 (82.5) | 49 (86.0) | 8 (14.0.) | - | 33 (57.9) | 20 (35.1) | 2 (3.5) | 2 (3.5) |
| Gastric acid suppression | 77 (10.6) | 53 (68.8) | 70 (90.9) | 4 (5.2) | 3 (3.9) | 41 (53.2) | 30 (39.0) | 3 (3.9) | 3 (3.9) |
| Oral antidiabetics | 38 (5.2) | 33 (86.8) | 35 (92.1) | 3 (7.9) | - | 20 (52.6) | 16 (42.1) | 2 (5.3) | - |
| Insulin | 4 (0.6) | 2 (50.0) | 3 (75.0) | 1 (25.0) | - | 2 (50.0) | 2 (50.0) | - | - |
| Opioid analgesics | 28 (3.9) | 10 (35.7) | 19 (67.0) | 4 (14.3) | 5 (17.9) | 15 (53.6) | 3 (10.7) | 7 (25.0) | 3 (10.7) |
| Non-opioid analgesics | 21 (2.9) | 6 (28.6) | 15 (71.4) | 2 (9.5) | 4 (19.0) | 10 (47.6) | 4 (19.0) | 3 (14.3) | 4 (19.0) |
| Oral steroids | 5 (0.7) | 4 (80.0) | 1 (20.0) | 4 (80.0) | - | 1 (20.0) | 4 (80.0) | - | - |
| Laxatives | 18 (2.5) | 3 (16.7) | 9 (50.0) | 2 (11.1) | 7 (38.9) | 6 (33.3) | 5 (27.8) | 6 (33.3) | 1 (5.6) |
| Antiepileptics/drugs for neuropathic pain | 3 (0.4) | 1 (33.3) | 2 (66.7) | 1 (33.3) | - | 3 (100) | - | - | - |
| Antibiotics | 6 (0.8) | - | 2 (33.3) | 3 (50.0) | 1 (16.7) | 1 (16.7) | 1 (16.7) | 2 (33.3) | 2 (33.3) |
| Anti-arrhythmic medications | 4 (0.6) | 1 (25.0) | 4 (100) | - | - | 4 (100) | - | - | - |
| Sedatives | 10 (1.4) | 5 (50.0) | 8 (80.0) | 1 (10.0) | 1 (10.0) | 5 (50.0) | 3 (30.0) | 1 (10.0) | 1 (10.0) |
| Antidepressants/ antipsychotics | 6 (0.8) | 4 (66.7) | 5 (83.3) | 1 (16.7) | - | 5 (83.3) | - | - | 1 (16.7) |
| Urogenital medications | 21 (2.9) | 18 (85.7) | 20 (95.2) | 1 (4.8) | - | 11 (52.4) | 9 (42.9) | 1 (4.8) | - |
| Pulmonary medications (inhaled medications) | 28 (3.9) | 15 (53.6) | 17 (60.7) | 4 (14.3) | 7 (25.0) | 5 (17.9) | 10 (35.7) | 12 (42.9) | 1 (3.6) |
| Other | 113 (15.6) | 46 (40.7) | 60 (53.1) | 24 (21.2) | 29 (25.7) | 49 (42.4) | 23 (20.4) | 30 (26.5) | 11 (9.7) |

Abbreviations: PIM – Potentially inappropriate medication; MDT – Multidisciplinary Team; n/a – not applicable

*percentage of all recommendations within drug class

## Discussion

We introduced a new care pathway for older adults who started with a new cancer therapy for advanced cancer and who had a limited life expectancy and used the results to study occurrence of DRPs and PIMs. This study shows that DRPs are very frequent in this population. Of all the medications a patient used, on average, 29% was potentially inappropriate and a median of six DRPs and three PIMs per patient were observed. None of the patient characteristics were associated with DRPs or PIMs, apart from the number of medications. The interview with the pharmacist revealed a substantial part of the DRPs, namely the majority of DRPs in the categories (possible) ADR, noncompliance, drug ineffective, and other, and 9% of DRPs was resolved during the interview.

We identified six DRPs per patient, which is more than the three DRPs found by Choukroun et al. [22] and the 1.7 DRPs found by Vrijkorte et al. [18]. This difference could be explained by differences in patient selection. In the study of Choukroun et al., 80% of the patients had polypharmacy and only 42% had metastatic cancer and although Vrijkorte et al. did select patients with polypharmacy, they did not include life expectancy as a selection criterion. As a result, our population likely had a shorter life expectancy, and we may have kept stricter criteria for other factors, such as overtreatment.

Overtreatment was the most common DRP, probably because it may not always be identified during regular care. Although an actual indication for the medication prescribed seems present when considering the patient history, treatment goals are not met when considering the decreased life expectancy.

In our study, the average patient had three PIMs. This is in line with other investigators, who also identified three PIMs in older adults with cancer [23]. Van Loveren et al. found only 1.2 PIM [17], but Whitman et al. found as many as five [24]. Patients in this last study, however, included substantially more over-the-counter medications and complementary and alternative medicines. These non-prescription medications accounted for 36% of all medications and in our study the proportion of non-prescription medications was only 8%. The effectiveness of non-prescription medications – in particular vitamins and alternative medicines – is less well established than the effectiveness of regular medications. As non-prescription medications were the most frequently deprescribed medications in that study, the large proportion of these medications could explain the higher number of PIMs found by Whitman et al.

The oncologist implemented 53% of the recommendations of the multidisciplinary team. Forty-six percent of the pharmacist's recommendations that were discussed in the multidisciplinary team were implemented by the oncologist. Other studies report 29 – 46% [18, 23, 25]. Pruskowski et al. focused on the acceptance of recommendations to discontinue medication and found that 64% of the recommendations were ignored and 8% rejected [25]. Frequently, the reason for not implementing a recommendation was not mentioned in the electronic medical record of the patient. The chart revealed that the recommendations coincided with more urgent matters requiring the oncologist's attention, such as early disease progression, severe chemotherapy-related toxicity, or presentation at the emergency ward. Recommendations about other medications were probably considered not urgent at those times and were subsequently forgotten. Other reasons for not actioning the recommendations were that the patient did not agree, that the oncologist held a different

clinical view, or that – especially during busy moments – changing certain types of medications were considered a task for the general practitioner.

We did not specifically record the number of medications before and after the intervention, as our medication optimization intervention was broader than just a deprescribing intervention. However, of all recommendations that advised deprescribing a PIM, 57% were accepted. On average, 1.7 PIMs were reduced per patient, which is less than the reduction of 2.6 - 4.4 medications that other researchers achieved [13, 14, 24, 26]. This difference may be explained by the differences in the populations studied, as few studies addressed patients with cancer. For example, as many participants in our study used opioid analgesics for cancer-related pain, laxatives were rarely discontinued. Likewise, antiplatelet drugs were rarely discontinued in our participants when no adverse drug reactions were mentioned because of the thrombogenic nature of cancer. Also, calcium supplementation was continued as a necessary part of the treatment of bone metastases with bisphosphonates or denosumab.

Patients were satisfied with the intervention overall. Regularly, patients indicated during the interview that they valued a thorough analysis of their medications. At the start of the interview with the pharmacist, the patients were asked about their attitudes towards their medication in general. Many patients answered that they wondered whether all those medications were still necessary and that they would be willing to discontinue medications if their doctor would agree.

The higher representation of male patients compared to female patients in our study is related to the distribution of cancer in the Dutch population. Apart from skin cancer, the most frequent cancers are prostate cancer, breast cancer, colorectal cancer, and lung cancer. Colorectal cancer and lung cancer occur more frequently in men and the number of women with breast cancer in the older population is much lower than that of prostate cancer in men [27]. As cardiovascular morbidity is more common in men, as is polypharmacy.

*Implications for Practice*

This study shows that a medication optimization care pathway supported by medication reviews and a multidisciplinary team meeting in older adults with cancer and a limited life expectancy is feasible and much appreciated by patients. Reducing DRPs should be an integral part of the approach of every health care professional involved in the care for these patients. We implemented a three-step model in the medication optimization intervention, in which a pharmacists performed the patient interview and the review of the medication.

The oncologist implemented a relatively high proportion of the recommendations that were given by the multidisciplinary team. Yet, a substantial proportion of the recommendations were not implemented by the oncologist, frequently due to practical reasons instead of an active and considered rejection by the oncologist. The implementation of the recommendations would probably increase if it were possible to introduce a system with reminders for the oncologist. Furthermore, the interviews provided much information on DRPs that cannot be extracted from the medical records. In our opinion a patient interview is an essential part of a medication optimization intervention and resolving DRPs could have an impact on quality of life. However, even without a patient interview, at least half of the DRPs or PIMs can be addressed [17, 18] by using a tool like OncPal to identify potentially inappropriate medication in palliative cancer patients [28]. Although the yield will be less than

with our method, this would likely still contribute to the quality of life of the patients and can be implemented more easily in lower- and middle-income countries.

*Strengths and Limitations*

The way the medication optimization care pathway was organized is a strength of this study. By combining the knowledge of oncologists, geriatricians, and pharmacists, the recommendations regarding medication are tailored to fit individual patients in the best possible way. Another strength of this study is that the study population is an accurate representation of the population treated for cancer in a general hospital.

A limitation of this study is the fact that this is a single center study, which may limit extrapolation to other centers. Furthermore, the study originated from an improvement of the usual care and, as a result, lacks a control group. We did not measure the impact of the intervention on the quality of life of the patients, although that would be an outcome of interest. We considered it infeasible to measure the impact on the quality of life, as too many other factors are involved, such as the start of chemotherapy with its associated toxicity or a decline in health due to disease progression.

*Future Research*

The evidence for deprescribing is scant. More research is needed on how to deprescribe preventive medications and which target values are acceptable regarding a certain remaining life span. The effect on the frequency of visits to the emergency ward and on medication-related hospital admissions should be investigated to study the cost-effectiveness of the medication reviews. Furthermore, the impact of this type of medication review on the quality of life and the effects of medication-related interventions on the emotional wellbeing of the patient should be investigated. Depending on the local situation and cooperation between hospital clinicians and primary caregivers, involving primary caregivers could be a viable approach to increase the uptake of recommendations and should be investigated.

## Conclusions

DRPs and PIMs are highly prevalent in older patients with advanced cancer starting a new cancer therapy and can be reduced by a multidisciplinary medication optimization intervention. Patients appreciate the medication optimization intervention and are satisfied with it.

## References


1. Siegel, R.L., K.D. Miller, and A. Jemal, *Cancer Statistics, 2017.* CA Cancer J Clin, 2017. **67**(1): p. 7-30.
2. Edwards, B.K., et al., *Annual Report to the Nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer.* Cancer, 2014. **120**(9): p. 1290-314.
3. Miller, M.G., et al., *Identifying potentially inappropriate medication (PIM) use in geriatric oncology.* J Geriatr Oncol, 2021. **12**(1): p. 34-40.
4. Schenker, Y., et al., *Associations Between Polypharmacy, Symptom Burden, and Quality of Life in Patients with Advanced, Life-Limiting Illness.* Journal of general internal medicine, 2019. **34**(4): p. 559-566.
5. Sevilla-Sanchez, D., et al., *Adverse drug events in patients with advanced chronic conditions who have a prognosis of limited life expectancy at hospital admission.* European journal of clinical pharmacology, 2017. **73**(1): p. 79-89.
6. LeBlanc, T.W., et al., *Polypharmacy in patients with advanced cancer and the role of medication discontinuation.* The Lancet Oncology, 2015. **16**(7): p. e333-e341.
7. Alkan, A., et al., *Severe drug interactions and potentially inappropriate medication usage in elderly cancer patients.* Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer, 2017. **25**(1): p. 229-236.
8. Deliens, C., et al., *Drugs prescribed for patients hospitalized in a geriatric oncology unit: Potentially inappropriate medications and impact of a clinical pharmacist.* Journal of geriatric oncology, 2016. **7**(6): p. 463-470.
9. Lund, J.L., et al., *Potential Medication-Related Problems in Older Breast, Colon, and Lung Cancer Patients in the United States.* Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 2018. **27**(1): p. 41-49.
10. Paksoy, C., et al., *Evaluation of potentially inappropriate medication utilization in elderly patients with cancer at outpatient oncology unit.* Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners, 2019. **25**(6): p. 1321-1327.
11. Brokaar, E.J., et al., *Deprescribing in Older Adults With Cancer and Limited Life Expectancy: An Integrative Review.* Am J Hosp Palliat Care, 2022. **39**(1): p. 86-100.
12. Garfinkel, D. and D. Mangin, *Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy.* Arch Intern Med, 2010. **170**(18): p. 1648-54.
13. McKean, M., P. Pillans, and I.A. Scott, *A medication review and deprescribing method for hospitalised older patients receiving multiple medications.* Intern Med J, 2016. **46**(1): p. 35-42.
14. Potter, K., et al., *Deprescribing in Frail Older People: A Randomised Controlled Trial.* PLoS One, 2016. **11**(3): p. e0149984.
15. By the American Geriatrics Society Beers Criteria Update Expert, P., *American Geriatrics Society 2019 Updated AGS Beers Criteria(R) for Potentially Inappropriate Medication Use in Older Adults.* J Am Geriatr Soc, 2019. **67**(4): p. 674-694.
16. O'Mahony, D., et al., *STOPP/START criteria for potentially inappropriate prescribing in older people: version 2.* Age Ageing, 2015. **44**(2): p. 213-8.

17. van Loveren, F., et al., *Prevalence and follow-up of potentially inappropriate medication and potentially omitted medication in older patients with cancer - The PIM POM study.* J Geriatr Oncol, 2021. **12**(1): p. 80-84.
18. Vrijkorte, E., et al., *Optimising pharmacotherapy in older cancer patients with polypharmacy.* Eur J Cancer Care (Engl), 2020. **29**(1): p. e13185.
19. Cipolle, R.J., Strand, L.M., Morley, P.C., *Pharmaceutical Care Practice*, ed. McGraw-Hill. 1998, New York: Health Professions Division.
20. Bellera, C.A., et al., *Screening older cancer patients: first evaluation of the G-8 geriatric screening tool.* Ann Oncol, 2012. **23**(8): p. 2166-2172.
21. Piccirillo, J.F., et al., *Prognostic importance of comorbidity in a hospital-based cancer registry.* JAMA, 2004. **291**(20): p. 2441-7.
22. Choukroun, C., et al., *Impact of a pharmacist and geriatrician medication review on drug-related problems in older outpatients with cancer.* J Geriatr Oncol, 2021. **12**(1): p. 57-63.
23. Nightingale, G., et al., *Implementing a pharmacist-led, individualized medication assessment and planning (iMAP) intervention to reduce medication related problems among older adults with cancer.* J Geriatr Oncol, 2017. **8**(4): p. 296-302.
24. Whitman, A., et al., *Pharmacist-led medication assessment and deprescribing intervention for older adults with cancer and polypharmacy: a pilot study.* Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer, 2018. **26**(12): p. 4105-4113.
25. Pruskowski, J. and S.M. Handler, *The DE-PHARM Project: A Pharmacist-Driven Deprescribing Initiative in a Nursing Facility.* The Consultant pharmacist : the journal of the American Society of Consultant Pharmacists, 2017. **32**(8): p. 468-478.
26. Curtin, D., et al., *Deprescribing in Older People Approaching End of Life: A Randomized Controlled Trial Using STOPPFrail Criteria.* Journal of the American Geriatrics Society, 2019: p. 10.1111/jgs.16278.
27. IKNL. *NKR Cijfers*. 2023 13-07-2023]; Incidence of gatrointestinal cancers in patients >60 years in 2016-2020]. Available from: https://iknl.nl/nkr-cijfers.
28. Lindsay, J., et al., *The development and evaluation of an oncological palliative care deprescribing guideline: the 'OncPal deprescribing guideline'.* Support Care Cancer, 2015. **23**(1): p. 71-8.

## Supplementary

*Appendix I. Patient Satisfaction Questionnaire*

Did your medication change as a result of the medication interview? yes / no

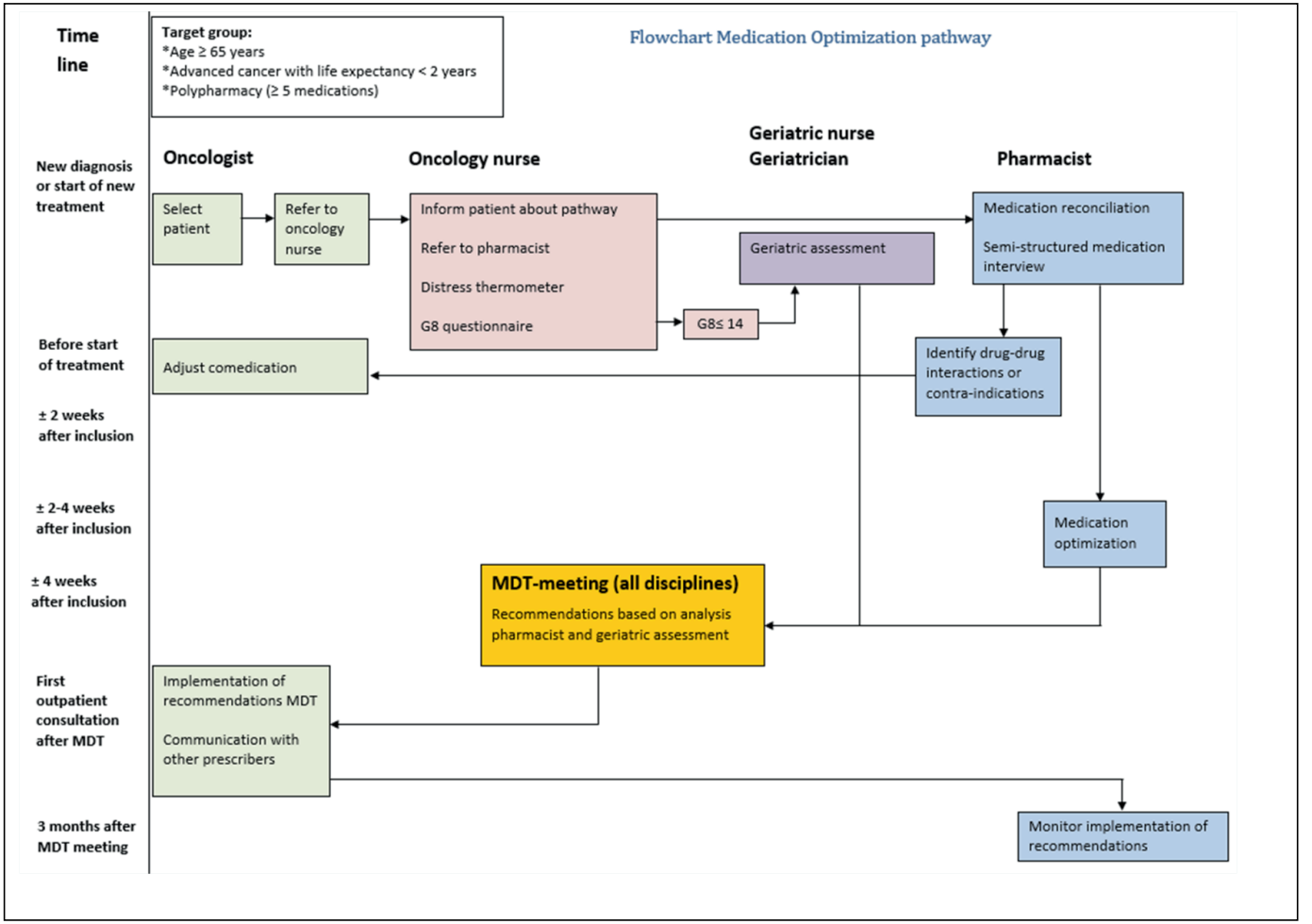
Were you anxious to change your medications? yes / no / a bit

| | VERY DISSATISFIED | DISSATISFIED | NEUTRAL | SATISFIED | VERY SATISFIED |
|---|---|---|---|---|---|
| How satisfied are you with the changes in your medication? | 1 | 2 | 3 | 4 | 5 |
| How satisfied are you with the medication interview? | 1 | 2 | 3 | 4 | 5 |
| How satisfied are you with the competence of the pharmacist? | 1 | 2 | 3 | 4 | 5 |
| How satisfied are you with your own involvement on making on possible changes in your medication? | 1 | 2 | 3 | 4 | 5 |
| How satisfied are you with the information you received about your medication? | 1 | 2 | 3 | 4 | 5 |

**Additional remarks**

*Appendix II. Categories of recommendations*

Stop drug
Add drug
Switch to other drug
Reduce dose
Increase dose
Alter frequency of administration
Alter route of administration
Monitor effect or ADR
Instructions for use/patient education
Reconsider treatment
Maintain treatment


Time line
Target group:
*Age ≥ 65 years
*Advanced cancer with life expectancy < 2 years
*Polypharmacy (≥ 5 medications)
Flowchart Medication Optimization pathway
Oncologist
Oncology nurse
Geriatric nurse
Geriatrician
Pharmacist
New diagnosis or start of new treatment
Select patient
Refer to oncology nurse
Inform patient about pathway
Refer to pharmacist
Distress thermometer
G8 questionnaire
G8≤ 14
Geriatric assessment
Medication reconciliation
Semi-structured medication interview
Before start of treatment
Adjust comedication
Identify drug-drug interactions or contra-indications
± 2 weeks after inclusion
± 2-4 weeks after inclusion
Medication optimization
± 4 weeks after inclusion
MDT-meeting (all disciplines)
Recommendations based on analysis pharmacist and geriatric assessment
First outpatient consultation after MDT
Implementation of recommendations MDT
Communication with other prescribers
3 months after MDT meeting
Monitor implementation of recommendations