Medication optimisation in older adults with cancer

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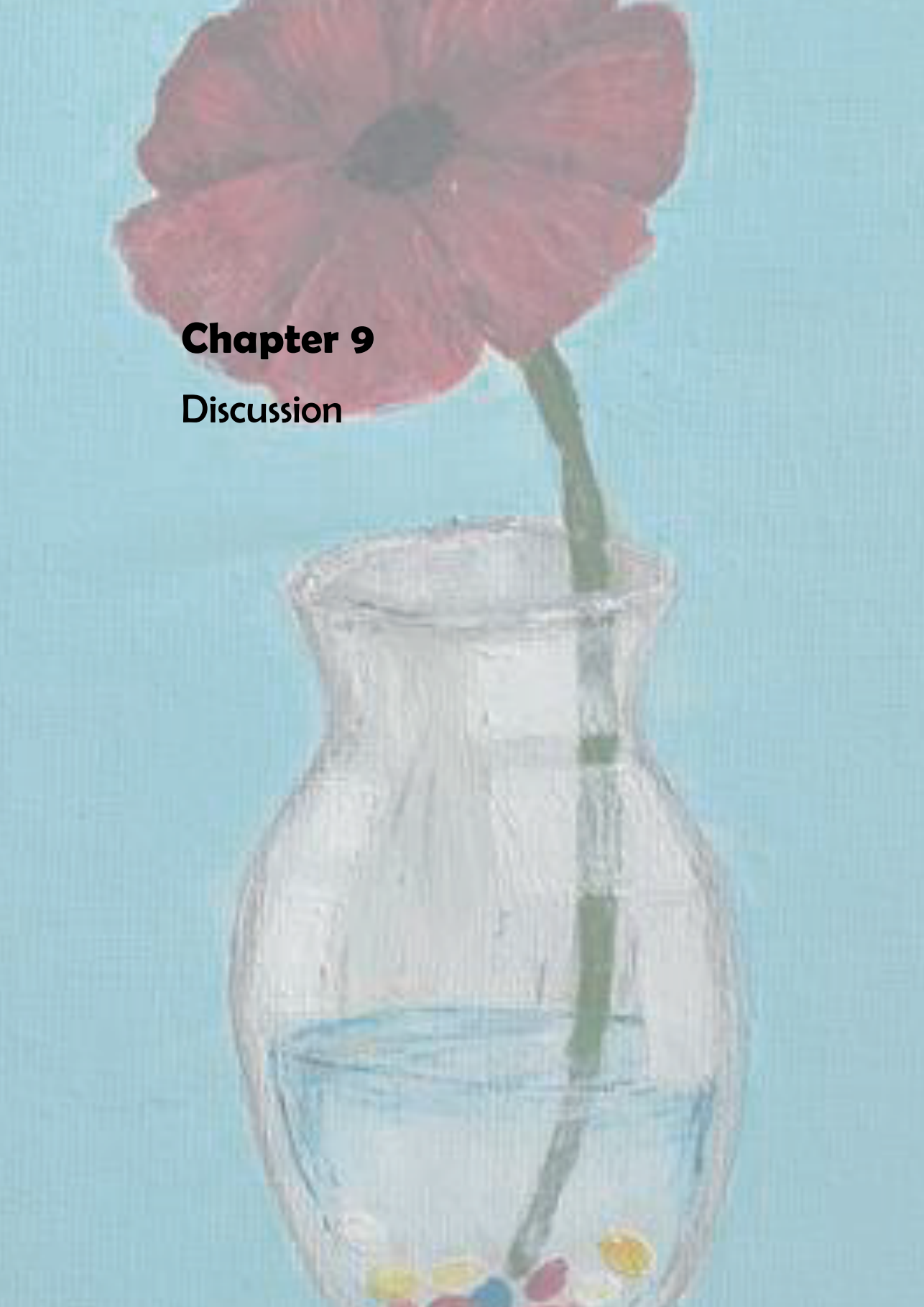

Chapter 9

Discussion

In the Introduction of this thesis, I described the case of Mr Smith. Could some of his problems have been prevented with a pharmacist participating in the multidisciplinary oncology team?

The absolute number of older adults with cancer has been steadily increasing in recent years, as has the proportion of older adults within the total cancer patient population. As a result, more research has been aimed at personalizing cancer treatment for older adults. Apart from decisions about the cancer treatment, problems related to other medications also require attention. This thesis addresses the identification of medication-related problems in older adults with cancer who receive a systemic anti-cancer treatment. Therefore, we studied various medication-related topics that are relevant for this growing group of patients.

This thesis has 4 key findings.

- Drug-related problems and potentially inappropriate medications are highly prevalent in older adults with cancer and a poor prognosis. These can be reduced by half by implementing a multidisciplinary medication optimization intervention.
- Discontinuation of commonly used preventive medications does not result in serious adverse events or decreased survival in vulnerable older patients.
- Potentially relevant herb-drug interactions between herbal supplements and oncological treatment occur in 4 % of older adults with cancer. Half of these herb-drug interactions are clinically relevant, yet many patients are unaware of this risk even if they use herbal supplements.
- The anticholinergic burden of medications is associated with poorer outcomes in older adults with cancer who receive systemic therapy. It is an independent risk factor for toxicity, additional to the risk of frailty that is already known.

Oncology pharmacists have been involved in the care for patients with cancer for several decades and their role is increasing. The key findings of this thesis provide ground to further expand their role for older cancer population specifically. Oncology pharmacists could play a vital role in medication optimization in this patient group. Performing a medication review in patients with a new cancer diagnosis enables discussion of various drug related problems. Potentially inappropriate medications could be identified and recommendations made for the oncologist about discontinuation of such drugs. Optimal recommendations require communication between pharmacist and oncologist about prognosis and treatment. Early recognition and discussion of medication related problems can prevent adverse events and improve quality of life of patients with cancer.
Physicians may be triggered when consulting a frail patient to re-evaluate the medication in use. However, patients with advanced cancer often are not frail at the beginning of the anti-cancer treatment, although the majority will live even shorter than the average frail older adult. Our study shows that patients with advanced cancer are willing to discontinue preventive medications.

Several complicating factors have to be addressed regarding the medication optimization intervention described in Chapter 3. First, it requires a substantial time investment from the pharmacist. Guidelines used in primary care for medication optimizations do not readily apply because of the often more limited life expectancy of the patients studied. Life expectancy is not easily predicted and may vary substantially even within cancer types and stages. This makes it difficult to make recommendations regarding the discontinuation of preventive

medication, due to the uncertainty about the potential benefits and risks of stopping, especially in patients who do not experience side effects.
Tools such as the OncPal criteria and the STOPP-FRAIL criteria can offer valuable support by reducing the time needed to identify medications that are typically suitable for discontinuation. Nevertheless, each recommendation still requires careful individual consideration, tailored to the specific patient sitting across from the healthcare provider.
Another complicating factor in deprescribing is the patient's own preferences. While a healthcare provider may judge that a particular medication no longer contributes meaningfully to a patient's wellbeing, the patient may prefer otherwise. The sense of security that some patients derive from long-standing medications can outweigh the clinical rationale for stopping them. Moreover, communicating that preventive medication can be discontinued must be done sensitively, as such information may confront patients with their limited life expectancy and approaching end of life.
A third challenge is the time investment required, which raises questions about the cost-effectiveness of the intervention. An experienced pharmacist needs roughly one hour to complete all steps of a medication review — from preparation and patient interview to formulating recommendations and discussing them with the oncologist. In our study, an average of 1.5 medications was discontinued, and the median survival of patients was nine months. Given that medication costs in the Netherlands are generally low, the financial savings from discontinuing these medications amount to no more than approximately €50. This means that cost-effectiveness must be demonstrated in areas other than direct reductions in medication expenditure.
One particularly relevant aspect is the potential improvement in quality of life for patients who undergo a medication review, although this is difficult to measure in the context of progressive disease and concurrent chemotherapy. It is also conceivable that stopping certain medications may reduce emergency care visits by preventing adverse events such as electrolyte disturbances, which would represent a meaningful and clinically relevant cost saving.

An integral part of a medication optimization intervention is verification of the use of over-the-counter medication and herbal supplements. These preparations usually are not registered in the medical records of the oncologist of pharmacist and, therefore, are not taken into consideration. We need to raise the question whether extensive assessment of herb use should be part of routine oncology care. Although only 12% of patients in our hospital cohort used herbs, in other populations herbal medications may be more prevalent. Therefore, inquiring after the use of herbal supplements should be an integral part of medication review. It could be more time-effective if a list is be drawn up with a number of frequently used herbs that have a known interaction with oncological medications. Such a list may also be readily accessible by the oncologist or specialized nurse for a swift handling of the herb-drug interaction. For rarer herb-drug combinations that are not on the list, the pharmacist can be consulted for evaluation and a recommendation. Using such a step-wise approach, relevant combinations can be identified and handled in the most efficient way.

The present role of oncology pharmacists is still strongly focused on the anti-cancer treatment and includes preparation and administration of anti-cancer drugs. However, in future they may also be involved in preventing toxicity of chemotherapy or adaptation of treatment schedules to improve treatment adherence and outcomes in frail older patients. In our

fluoropyrimidine study, toxicity and/or dose reduction, cycle delay, cycle interruption or early treatment discontinuation were associated with polychemotherapy regimens and full dose treatment. In addition, patients with high anticholinergic burden, an indicator for the possible presence of frailty, had poorer outcomes. Older patients more frequently require deintensification of anti-cancer treatment, It could be argued that instead of regular treatment with subsequent dose mitigations, a reverse approach may lead to a more tolerable treatment. Using a "start-low, go-slow" strategy, patients start with upfront dose reduction that is followed by dose escalation when treatment is tolerated well. It would be interesting and even required to study whether a start-low go-slow approach will in fact lead to fewer treatment discontinuations, less toxicity and of course no decrease in survival. Due to the impact of lower grade toxicity in frail older adults, grade 1-2 toxicity and/or quality of life should be studied as well.

Future perspectives

The studies in this thesis underscore the contribution of a pharmacist to the oncology team. For oncologists and oncology nurses, medication-related issues are just a part of the entire package of care provided to patients with cancer. For pharmacists, medication is their specialty. Therefore, pharmacists should be part of the oncology core team or as allied health professionals, comparable to geriatricians, physiotherapists, psychologists, or dieticians. The core oncology team should refer patients to pharmacists when applicable. Our medication optimization intervention study and herb-drug interactions study are practical and useful examples of how a pharmacist can contribute to the improvement of care for older adults with cancer.

A suitable approach to enrich the role of the oncology pharmacist could be to implement a care pathway similar to the one we described in Chapter 3. Such a medication optimization process does imply a medication reconciliation and lends itself well to inquiring after the use of herbal supplements for risk assessment as well. Furthermore, the use of herbal supplements may expose health-related issues or questions the patients does not discuss with their oncologist spontaneously and which may then be addressed properly. Also, the oncology pharmacist will be able to provide correct information on the reasons for or belief about the usefulness of herbal supplements.

Furthermore, involvement of oncology pharmacists improves safety by reducing adverse drug reactions and potential medication errors. The oncology pharmacist may especially improve care for older patients with comorbidities and polypharmacy. Oncology pharmacists, should be able to combine geriatric pharmacy with oncology care and integrate these two aspect to serve the older cancer patient more holistically, based on their specific needs.

Probably the most difficult aspect of the process was the implementation of recommendations. A dedicated oncology pharmacist can keep track of all recommendations and follow these up. In addition, an oncology pharmacist can secure continuity of care in the communication about medication between oncology team, general practitioner and other prescribers. An oncology pharmacist has the knowledge to address medication-related problems from both anti-cancer medications and regular medications with the involved physicians. Also, the oncology pharmacist could continue to be a sparring partner for the general practitioner on medication-related issues once anti-cancer treatment is ceased and the patient is referred back to primary care. As involvement of the oncology pharmacist starts

shortly after diagnosis or initiation of anti-cancer treatment, advanced care planning can be enriched with specific medication-related recommendations.
The medication optimization intervention described in this thesis focusses on older adults with cancer and a poor prognosis. However, patients with a better prognosis may benefit from a medication optimization as well. For those patients, a medication optimization may not be a one-time action, but could be incorporated in the regular cancer care. A medication optimization can be performed for example yearly or when progression significantly alter the prognosis of the patient.

A means to increase effectiveness may be a work-flow comparable to that of a pharmacist-consultant in general practice clinic. Such a pharmacist-consultant acts more like an independent prescriber than as an advisor of the general practitioner. Instead of merely advising the general practitioner on adjustments to the medication, a pharmacist-consultant implements alterations independently and does the required follow-up. In a similar way, an oncology pharmacist-consultant could make adjustments to the medication after consensus in the MDT meeting and subsequently evaluate the effect of the interventions. Adding a pharmacist to the multidisciplinary oncology team can significantly improve patient care without increasing the workload of current oncology teams.