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Medication optimisation in older adults with cancer

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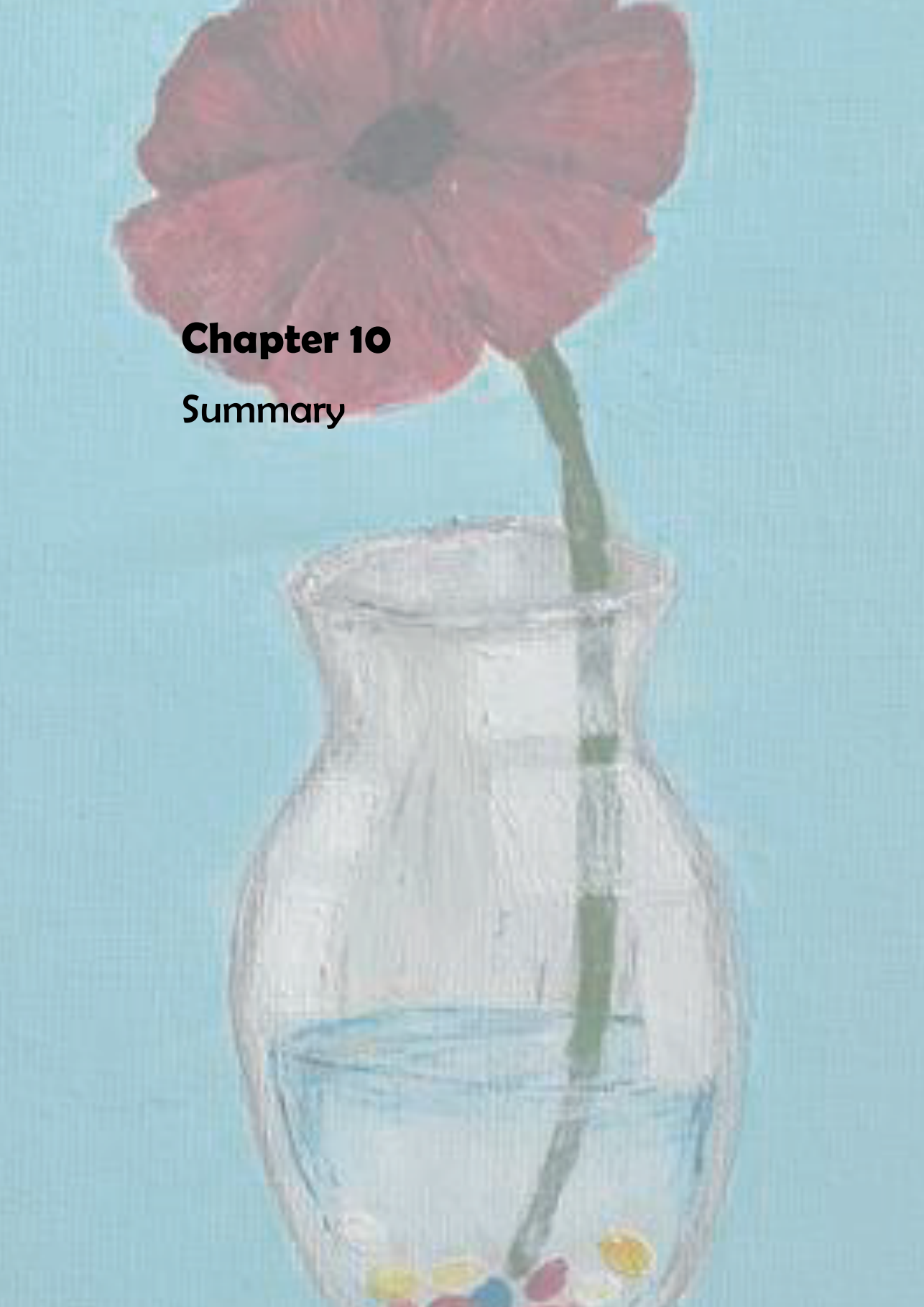

Chapter 10

Summary

In this thesis, we investigate various aspects related to medication in older adults with cancer who receive systemic anti-cancer therapy and how the role of oncology pharmacists can be expanded in the care for this patient group.

The literature review in Chapter 2 showed that various medication groups that have been beneficial previously, may become redundant for patients with a limited life expectancy. Several good quality studies indicate that discontinuing bisphosphonates for osteoporosis and supplementation of calcium and vitamin D is safe and without adverse events. Lipid lowering drugs can be deprescribed safely and this may even improve quality of life. Furthermore, antihypertensive drugs and antihyperglycemic drugs can be discontinued safely in a considerable part of older patients with a limited life expectancy. Reintroduction at the recurrence of symptoms will occur in a minority of patients only. Discontinuation of these drugs in vulnerable older patients did not result in serious adverse events or decreased survival.

In Chapter 3 we described the results of a medication optimization intervention in older adults with cancer, starting a palliative systemic therapy and a life expectancy under 2 years. Although this study was performed in a single center, the population is representative of the cancer population in a general hospital. We showed that on average 6 drug-related problems occurred and 3 potentially inappropriate medications were in use per patient and that a 50% reduction can be achieved with a medication optimization intervention. Overtreatment occurred in 26% of patients. Preventing overtreatment requires clinical reasoning and collaboration between pharmacist and treating physician. Although guidelines may mention deprescribing medication for frail patients or patients with a limited life expectancy, re-evaluating current medication usually does not occur when a life-limiting cancer is diagnosed and time to effect becomes relevant. Due to various patient- and cancer-related variables, defining overtreatment based on general – long-term – treatment goals is a delicate process in which patient preferences should be incorporated as well.
Patient preferences can only be obtained by engaging with the patient, which is also very important for identifying drug-related problems. Although many drug related problems can be identified using medical and pharmaceutical records, as many as 21% of drug-related problems were only identified by means of the patient interview. Often, these were adverse drug reactions and resolving those issues contributes significantly to the quality of life.
Overall satisfaction about the medication-optimization intervention was high and the implementation rate of 53% for the recommendations was high compared to similar studies, but room for improvement exists. Approximately one-third of the recommendations was ignored. The oncologist did not explicitly reject the recommendation, but it was just lost over time in the medical record. This has to do with the structure of the medical records, in which all recommendations are presented in one report in the medical record. Once a few new entries are made, the report disappears off screen and will only be found when searched for. A system in which the oncologist easily could execute, reject or postpone each recommendation would improve the uptake.

In Chapter 4, we observed that 23% of older adults with wild type *DPYD*-genotype experienced grade ≥3 toxicity. Yet, for older adults even less severe toxicity may impact quality of life to such an extent that mitigation of treatment is warranted. Therefore, we also studied the composite endpoint composed of grade ≥3 toxicity and/or dose reduction, cycle delay, cycle

interruption or early treatment discontinuation. Forty-one percent of patients experienced this composite endpoint. This highlights that for many patients, who do not experience grade ≥3 toxicity, treatment with fluoropyrimidines nevertheless affects their life to such an extent that they cannot complete the chemotherapy course as intended.
Unlike expected, severe toxicity was not associated with frailty characteristics, but the composite endpoint was associated with high cancer stage, polychemotherapy and high dose range.

In Chapter 5 we demonstrated that 12% of older adults use herbal medication alongside systemic therapy for cancer, 4% with potential for herb-drug interaction. Following assessment by a pharmacist, half of these herbal medications were indeed contraindicated because of relevant herb-drug interactions and led to a recommendation to discontinue. We found a variety of herbal supplements with potential herb-drug interactions being used. The most frequently used herbal supplements were red cone flower and cannabis, together accounting for nearly half of the herbs with a potential herb-drug interaction.
Strikingly, less than one third of patients were aware that herbal supplements may interact with regular anti-cancer treatment. However, 58% of patients who actually use herbal supplements, is aware of the possible interaction.

In Chapter 6 we investigated the association between the anticholinergic medication burden and the occurrence of severe toxicity. A high anticholinergic burden was present in 15% of patients and was associated with severe toxicity. The multivariable models revealed that both anticholinergic burden and frailty were associated with treatment toxicity. A high anticholinergic burden is an independent risk factor for toxicity, additional to the known risk of frailty.
Furthermore, anticholinergic medication burden was associated with functional decline at 12 months from the start of anti-cancer treatment and with ER-visits or hospitalization, both of which are relevant outcomes for patients who will undergo intensive treatment for cancer.

The findings of this thesis can lead to an increase in integral care for older adults that expands the classic role of oncology pharmacists and improve care for these patients beyond the systemic anti-cancer treatment.