Valorisation
In this thesis several studies based on patients with metastatic breast cancer in every day clinical practice are presented. The results are not only relevant for scientific purposes, but are also of importance from a societal and economical perspective. Breast cancer is a major global health issue with over 500 000 deaths annually. In the Netherlands, almost 16 000 patients were diagnosed with invasive breast cancer in the year 2015. Around 20% of all breast cancer patients will develop a distant recurrence after prior treatment of early stage breast cancer, and around 5% of patients are found to have metastatic breast cancer at initial diagnosis. Once distant recurrence has occurred the disease is generally incurable.

In the first study described in this thesis, we determined the median survival of patients with metastatic breast cancer, according to subgroup based on HER2 and hormone receptor status. The subgroup with the most favorable prognosis, the hormone receptor-positive/HER2-positive subgroup, had a median survival of 34.4 months, with a range up to more than 46.6 months. This shows that, even though metastatic breast cancer remains incurable, there are patients with metastatic breast cancer who will live many years after the diagnosis of metastatic breast cancer. During those years, these patients are most likely treated with several lines of therapy. This period has major implications for the patient and their families, as well as for society. First of all, the diagnosis and the uncertainty on prognosis and disease course can lead to feelings of isolation, worries and even depression in a third of women with advanced breast cancer at diagnosis. And these patients feel the need to have more information available on metastatic breast cancer at diagnosis, as well as during the course of their disease and treatment.

With the impact of metastatic breast cancer diagnosis and treatment on the quality of life, it is essential that we translate our scientific data to useful and personalized information to the patients and their families in every day clinical practice. One of the societal benefits from this thesis is the use of these data to help inform our patients with metastatic breast cancer in daily practice. Our data provide knowledge on anticipated disease course, which can help to make informed decisions on treatment and can prevent anxiety and uncertainty of the future once the diagnosis is determined.

Furthermore, more than half of patients with metastatic breast cancer experience a decline in income and, besides paid employment, many of the women with metastatic breast cancer participate in unpaid activities, such as cooking, household and taking care of children and/or relatives on which the disease has an impact as well. This so called ‘grey economy’ needs to be accounted for when examining the economic burden of metastatic breast cancer, in addition to the costs directly related to the disease, symptoms and treatment as well as costs related to loss of productivity.
This thesis is based on a large real-life cohort of patients in several hospitals in the Southeast part of the Netherlands. This is in contrast to most data on metastatic breast cancer, which are usually derived from randomized clinical trials. There is an added value of these real-life data, since in daily practice only a small percentage of metastatic breast cancer patients participate in randomized trials. Therefore, the objective of this thesis was to gather and analyze real-life data on disease course, prognostic factors and treatment allocation. Not only are these data needed to help inform patients and their treating physicians, but it can also help to determine efficacy, implementation and use of therapeutic regimens in real-life. This information has major implications for society, since it is needed to determine and improve the quality of care and estimate the cost-effectiveness of new drugs.

One of the future improvements should be the gathering of relevant real-life data in a way that is less time consuming and more integrated in every day clinical practice. In an era in which electronic medical records are commonly used in hospitals in the Netherlands and most Western Countries the possibilities of data collection and sharing are numerous. With less time on less costs involved in data collection, the results from these population-based studies should become available more quickly and could thus have a bigger impact on daily treatment, information provided to the patients with metastatic breast cancer and their quality of life. Since there is such an added value of real-life data, not only for patients and their treating physicians, but also for pharmaceutical industries and governments deciding on reimbursement and health care budgets and controlling quality of care, the efficacy of collection of the relevant data should be a joined effort of all involved fields in breast cancer care.

One of the examples of the value of real-life data comes from the study of this thesis exploring the first given treatment for patients with hormone-receptor positive metastatic breast cancer. Our study showed that nearly a quarter of patients started palliative treatment with chemotherapy, although it is recommended in the guidelines to start with endocrine treatment provided that the disease is not (extremely) aggressive. Our study does not only show that in real-life different treatment choices are made, it also implicates that real-life treatment choices in metastatic breast cancer are complex and that many factors play a role in the treatment decision-making process. These data are relevant when informing our patients on treatment options, but may also help to improve future decision-making. Data from the real-life population based studies can also help to guide the design of the randomized clinical trials, thereby resulting in more appropriate and thereby more efficient trial designs.

Another example concerns the use of bevacizumab, which was registered and approved for the treatment of metastatic breast cancer in 2008 based on randomized
clinical trial data. One of the studies of this thesis describes the implementation of bevacizumab hereafter. It was shown that bevacizumab was administered less often than anticipated and potentially indicated. Moreover, almost a quarter of patients receiving bevacizumab-taxane had no indication for bevacizumab or received this despite (relative) contraindication in real-life in the Netherlands. This study shows the importance of monitoring the daily use of a new therapeutic drug in daily practice to help guide optimal implementation and use of a new drug in according to guideline recommendations. This is essential in controlling quality of the provided cancer care and thereby improving the quality of life and outcome of patients with metastatic breast cancer.

Besides the implementation and thereby directly influencing the patients and their doctors, these real-life data are also of importance from an economic perspective. These new cancer drugs impose a substantial burden on our health care budget. Due to the introduction of new cancer drugs, the costs will continue to increase over the years. From a societal view, it is essential that these new drugs are properly implemented, limited to the patients who are expected to benefit the most. We observed, that patients who were in real-life selected for first-line bevacizumab-taxane treatment had a median progression-free survival of 6.0 months (95% CI 4.8-13.1). As aforementioned, the selection of patients was suboptimal. The addition of bevacizumab to a taxane for the first-line treatment of HER2-negative metastatic breast cancer was associated with an increase in costs of €56,213. Even though there was also an increase in quality-adjusted life years with the addition of bevacizumab of 0.362, the cost-effectiveness ratio amounted to €155,261 per quality-adjusted life years gained, which is not considered cost-effective in the Netherlands. Such information is essential for decisions on reimbursement as well as for the ongoing debate on how to manage the increasing health care expenditure.

In conclusion, this thesis provides essential data on metastatic breast cancer in real-life. One of the main goals of this thesis is to increase awareness about this important group of patients. We hope the results of the studies in this thesis will lead to a better understanding of prognostic and predictive factors, treatment patterns, disease course and outcome in patients with metastatic breast cancer. Furthermore, we hope these results will help stimulate more appropriate allocation of existing treatment options, and can be a starting point of new developments of treatment regimens for patients with metastatic breast cancer in the future. All with the ultimate goal to improve quality of care and outcome for patients with metastatic breast cancer.