Reducing throughput time until chemotherapy treatment

Master thesis

S.J. Veldhuizen
June 2014

NKI-AVL

UNIVERSITY OF TWENTE.

Reducing throughput time until chemotherapy treatment

S.J. Veldhuizen

Student number s0175447

June 2014

Master thesis

University of Twente

School of Management and Governance

Master programme Industrial Engineering and Management

Master track Production and Logistics Management

Author

Sjoerd Veldhuizen, BSc

Supervisors University of Twente

Dr. ir. M.E. Zonderland

Prof. dr. ir. E.W. Hans

Supervisors Antoni van Leeuwenhoek

Ir. J. Deetman

Dr. ir. W.A.M. van Lent

NKI-AVL

UNIVERSITY OF TWENTE.

Management summary

Dutch hospitals are increasingly transparent. Mortality rates and waiting time for treatments supply quantitative information on services. Hospital performance becomes more comparable which also applies to breast cancer treatment at the Antoni van Leeuwenhoek hospital. Management of this patient group is dissatisfied with current waiting times for neoadjuvant chemotherapy treatment (i.e. chemotherapy treatment prior to surgery). Although the process is not transparent and therefore little evidence is available, management regards the period of time between the start of the care pathway and the first chemotherapy treatment as too long. Various of tests and pre-assessments are required before chemotherapy can be dosed. Simultaneously, high utilisation of the corresponding capacities is desired. This research serves to determine the required capacity to start the chemotherapy treatment for at least 90% of the patients within two weeks and analyse the consequences for the utilisation.

Data analysis shows that performance significantly deviates from the desired situation. The current throughput time until the first chemotherapy treatment for at least 90% of the patients is 28 days and thus the service level is not attained. The average throughput time is 20 days. Waiting times for appointments prior to treatment are high since available capacity is shared with other patient groups and therefore varying. Especially appointments at the Nuclear Medicine department construct delay in the process. To improve performance, dedicated time slots are included.

In order to model the approach, a combination of queuing theory and discrete-event simulation is used. Time slot configurations are determined for different patient arrival scenarios. A configuration is regarded as the set of included time slots for all appointment types. Since high utilisation correlates with high waiting times, tradeoffs are inevitable. Utilisation of time slots must be significantly less than 100% to limit the waiting times.

The average utilisation of time slots for current patient arrivals is approximately 65% to satisfy the desired service level. Results show increased utilisation of time slots when more patients arrive. Nevertheless, utilisation is ought to be relatively low in order to start the treatment for at least 90% of the patients within two weeks. Utilisation of time slots is limited to approximately 85% in order to plan at least 90% of the appointments within two weeks. This means that an utilisation over 85% for a single appointment type causes the desired service level to be unattainable. As appointment planning restricts appointment sequencing, feasible utilisations might only be as high as 80%. A number of appointments are crucial to be planned at appropriate days since delay of appointments significantly delays the throughput time until the first chemotherapy treatment. This is caused by the appointment planning restrictions. The first appointment with a nurse practitioner, the MRI scan, the biopsy, the appointment with the internist and both the consult and first treatment at the Outpatient Clinic form this group.

Furthermore, time slots should be allocated with respect to patient arrival distributions and appointment planning restrictions. For example, the results of tests and pre-assessments are discussed with the internist and therefore impact the appropriateness of internist time slot scheduling. When time slots are incorrectly aligned, the service level decreases highly. The use of biweekly schedules enables more accurate alignment of capacity and demand. With biweekly schedules, utilisation can be set to approximately 80%, where weekly schedules are limited to either significantly lower or higher utilisations.

Moreover, the utilisation of time slots of appointments at the Nuclear Medicine department in particular is required to be high. Feasible utilisation of these appointments is limited by approximately 80%. Utilisation of time slots of an appointment type is regarded as feasible when the desired service can be achieved.

Although time slot allocation proves to be suitable to achieve the desired service level, consequences for other patient groups are not included in the model. As excessive capacity is required to cope with variations in demand, the availability of resources for other patient groups declines.

Finally, the applicability of planning appointments outside the time slots and releasing time slots is recommended to be researched. When appointments are allowed to be planned outside the time slots, required capacity can be decreased. This is a reasonable approach as long waiting times for appointments will be bypassed in reality. Releasing time slots at specified moments enables other patient groups to use the capacity and increases utilisation of time slots. Both approaches presumably improve the use of time slots.

Management samenvatting

Sinds een aantal jaren worden Nederlandse ziekenhuizen steeds transparanter over hun prestaties. Ze publiceren in toenemende mate sterftecijfers en wachttijden, waardoor patiënten hun keuze voor behandeling in een bepaald ziekenhuis op basis van kwantitatieve cijfers kunnen vergelijken. Een lange wachttijd voor behandeling in het Antoni van Leeuwenhoek ziekenhuis kan er dus toe leiden dat patiënten kiezen voor behandeling elders. In de ogen van het management van het Antoni van Leeuwenhoek ziekenhuis is de huidige doorlooptijd tot neoadjuvante chemotherapie voor borstkankerpatiënten te lang. Neoadjuvante chemotherapie vindt plaats voorafgaand aan de operatie. Hoewel het proces dat borstkankerpatiënten doorlopen niet inzichtelijk is en er geen cijfers beschikbaar zijn over de huidige prestatie, is het management ontevreden. Voorafgaand aan de behandeling met chemotherapie moeten een aantal afspraken gepland worden en zijn aanvullende diagnostische onderzoeken noodzakelijk. Het doel van dit onderzoek is het bepalen van de benodigde capaciteit om de behandeling met chemotherapie te kunnen starten binnen twee weken na binnenkomst bij minimaal 90% van de patiënten. Hiervoor is het noodzakelijk dat de afspraken voorafgaand aan de behandeling binnen twee weken kunnen plaatsvinden. Tegelijkertijd is een hoge bezettingsgraad gewenst.

Data analyse laat zien dat de huidige prestatie niet overeenkomt met de gewenste situatie. De doorlooptijd tot behandeling is momenteel maximaal 28 dagen voor 90% van de patiënten en gemiddeld duurt het 20 dagen voordat een patiënt start met de chemotherapiebehandeling. Patiënten moeten lang wachten voor diverse afspraken voorafgaand aan de behandeling. De capaciteit wordt gedeeld met andere patiëntengroepen waardoor de beschikbaarheid van de vraag van deze patiënten afhangt en sterk varieert. Met name de afspraken bij de afdeling Nucleaire Geneeskunde veroorzaken vertraging in de doorlooptijd tot behandeling. Om de gewenste doorlooptijden te realiseren onderzoeken we de toepassing van timeslots voor alle afspraken tot en met de eerste kuur.

Om te bepalen hoeveel timeslots nodig zijn voor elk afspraaktype, wordt een combinatie van een wachtrijmodel en simulatie gebruikt. Tijdslot configuraties worden bepaald voor verschillende patiëntenaantallen zodat mogelijke toekomstige situaties ook geanalyseerd worden. Een configuratie wordt beschouwd als het aantal gereserveerde timeslots voor elke afspraak. Omdat hoge bezetting gepaard gaat met hoge wachttijden, moeten afwegingen gemaakt worden.

Om 90% van de patiënten binnen twee weken te laten starten met de chemotherapie behandeling is de bezetting van timeslots gemiddeld 65%. De capaciteit kan effectiever benut worden wanneer meer patiënten dit 'zorgpad' gebruiken. De bezetting van timeslots is maximaal ongeveer 85% om minimaal 90% van de afspraken binnen twee weken te kunnen plannen. Dit betekent dat een bezetting van timeslots hoger dan 85% resulteert in het niet kunnen halen van de gewenste servicegraad. Doordat afspraken van elkaar afhankelijk zijn is de beschikbare periode waarin een afspraak gepland kan worden kleiner dan twee weken. Hierdoor is de toegestane bezetting geschat op maximaal 80%. Voor een aantal afspraken heeft een vertraging een lagere servicegraad tot gevolg. Dit wordt veroorzaakt door strakke planningsrestricties. Afspraken die hiertoe behoren zijn het eerste gesprek met een verpleegkundig specialist, de MRI scan, het biopt, de afspraak met een internist en zowel het consult op de dagbehandeling als de eerste kuur op de dagbehandeling.

Het is belangrijk dat timeslots schema’s gebaseerd worden op de wekelijkse verdeling waarin patiënten aankomen en op planningsrestricties. Zo worden de resultaten van de aanvullende diagnostische onderzoeken besproken met de internist, hetgeen timeslots voor internistafspraken beïnvloedt. Wanneer dit niet goed op elkaar afgestemd is, kan het zijn dat de afspraak met de internist niet plaats kan vinden omdat de resultaten van de aanvullende onderzoeken nog niet bekend zijn. Dit kan de doorlooptijd vertragen. Verder toont toepassing van tweewekelijkse schema’s aan dat de capaciteit beter kan worden afgestemd op de vraag. Waar bezetting van timeslots bij wekelijkse schema’s in sommige gevallen zeer laag of zeer hoog is, kan middels tweewekelijkse schema’s voor deze afspraken een geschikte bezetting gevonden worden.

Bovendien wordt een lage bezetting van timeslots voor afspraken op de afdeling Nucleaire Geneeskunde waarschijnlijk niet geaccepteerd. Experimenten tonen aan dat de maximale bezetting van timeslots ongeveer 80% zal zijn.

Hoewel het gebruik van timeslots geschikt is om de gewenste servicegraad te behalen, zijn de gevolgen voor andere patiëntengroepen niet bepaald. Met deze aanpak wordt meer capaciteit gevraagd door deze patiëntengroep dan momenteel het geval is, waardoor de beschikbare capaciteit voor andere patiëntengroepen afneemt.

Ten slotte wordt aanbevolen om te onderzoeken in hoeverre afspraken buiten timeslots om kunnen worden gepland. Wanneer dit geoorloofd is, wordt een hoge bezetting toelaatbaar aangezien lange wachttijden vermeden worden. Daarnaast wordt aanbevolen om de toepassing van het vrijgeven van timeslots te onderzoeken. Als timeslots vrijgegeven kunnen worden, hebben andere patiëntengroepen de mogelijkheid om deze capaciteit te benutten. Op deze manier zal de bezetting van timeslots verhoogd worden, wat resulteert in lagere wachttijden voor andere patiëntengroepen. De verwachting is dat beide aanbevelingen het toepassen van timeslots meer geschikt maken.

Preface

This master thesis is the result of my research into the reduction of the throughput time of a care pathway within a complex organisation. With this project, I complete my master programme Industrial Engineering and Management. I look back at a wonderful time as a student in the city of Enschede.

During my master, I became interested in the healthcare sector. Elective courses regarding healthcare processes fuelled my preference to graduate in a healthcare environment. A guest lecture of Wineke van Lent on behalf of the Antoni van Leeuwenhoek hospital appealed to me, which ultimately resulted in this graduation project. This project has been a great opportunity for me to get familiar with healthcare processes in a fascinating hospital. Furthermore, it was a great challenge to put in practice the knowledge I acquired during my studies.

Reflecting upon this research, I would like to thank some persons who contributed to my graduation. First of all, I express my gratitude to Joost Deetman and Wineke van Lent for the opportunity to perform this research in a complex and interesting organisation with highly devoted employees. In particular, I would like to thank Joost Deetman for his supervision and design of this graduation project. I would like to thank Wineke van Lent for her interest and thinking along. I really enjoyed my time at the Antoni van Leeuwenhoek hospital, for which I would like to thank my colleagues. Furthermore, I thank Jacqueline van Zyll de Jong for her contribution and willingness to help me, even though she believes that my research might make a significant part of her activities redundant.

Special thanks go to my supervisors of the University of Twente. I would like to thank Maartje Zonderland for her commitment and support to complete this research. Moreover, I would like to thank Erwin Hans for sharing insights in healthcare management and his help in structuring this graduation project.

Finally, I would like to express my gratitude towards my family and Sophie. Their love and support enabled me to complete this project and my studies.

Sjoerd Veldhuizen

Amsterdam, 2014

Contents

List of abbreviations

ATP	Additional tests and pre-assessments
AVL	Antoni van Leeuwenhoek
CP	Care pathway
CRX	Chest X-ray
ECG	Electrocardiography
ED	Emergency department
EF	Ejection Fraction
ER	Oestrogen receptor
GP	General practitioner
K-S	Kolmogorov-Smirnov
LP	Linear programming
MDP	Markov Decision Process
MDT	Multidisciplinary team
MRI	Magnetic resonance imaging
NCT	Neoadjuvant chemotherapy treatment
NP	Nurse practitioner
OC	Outpatient Clinic
OFAT	One-factor-at-a-time
OR/MS	Operations Research and Management Science
PET/CT	Positron emission tomography-computed tomography
POS	Preoperative Screening
PR	Progesterone receptor
SN	Sentinel Node
SNI	Sentinel Node Imaging
SNP	Sentinel Node Procedure

1 Introduction

Hospitals are increasingly transparent. Mortality rates and waiting times appear more often in the media. Hospitals currently publish performance on their websites, giving potential patients quantitative information whereupon they might select the hospitals at which they desire to be treated. This also applies for breast cancer treatment. As patient arrivals increase and competing hospitals show lower waiting times for chemotherapy, pressure is built to decrease the waiting time for chemotherapy at the Antoni van Leeuwenhoek hospital. However, at the same time utilisation of capacities is required to remain the same or even increase. These conflicting goals form the main issue cover in this thesis.

This chapter starts with a concise introduction to the Antoni van Leeuwenhoek hospital (Section 1.1). Section 1.2 describes the problem background followed by the problem identification in Section 1.3. Section 1.4 describes the objective and the research questions. Section 1.5 discusses the research approach. Section 1.6 completes this chapter by defining the scope of this research.

1.1 Introduction to the Antoni van Leeuwenhoek hospital

The goal of the Antoni van Leeuwenhoek hospital (AVL) is to offer the best treatments for cancer patients. AVL pursues this goal through the combination of patient care and research. Due to this specific focus, the hospital is valued among the best hospitals in the world in terms of cancer treatment. With 42,101 surgical procedures and 180 beds in 2012, AVL is a small sized Dutch hospital (http://www.avl.nl/).

Picture 1: Antoni van Leeuwenhoek hospital, Amsterdam (2010)

Management expects an increase in patient numbers in the coming years. The annual report of 2012 states an anticipated growth in patient numbers of 50 percent in the period between 2008 and 2020 (Jaardocument 2012). In 2012, the growth was beyond anticipations, which suggests that the 50 percent growth rate is underestimated. With the construction – that is currently being realised – of five additional operating theatres, dozens of extra beds (distributed over different departments) and numerous other expansions, a significant growth is enabled.

1.2 Problem background

Breast cancer is a cancer type that affects many people. It is the single most frequently occurring type of cancer among women in the Netherlands. The website of the Dutch Cancer Society KWF Kankerbestrijding (http://www.kwf.nl/) states that in 2012, 14,376 people were diagnosed with breast cancer in the Netherlands, of which a vast majority (99.44 percent) was female. Breast cancer patients form a significant part of patients treated in AVL.

Neoadjuvant chemotherapy care pathway

Patients arrive at the hospital with the suspicion of breast cancer. They are referred to AVL by their general practitioner (GP), possibly as a result of the breast cancer screening programme, or via another hospital. At this point, a tumour is not necessarily present nor malignant. Patients with abnormalities in the breast are subjected to diagnostic examinations at the outpatient breast clinic (the so called Mammapoli). The results of the examinations are discussed in a multidisciplinary team (MDT) which ascertains the diagnosis. Patients diagnosed with the presence of one or more malignant tumours are further treated while others terminate the process. Figure 1 on the next page shows the process of selecting the appropriate treatment plan for patients.

After breast cancer is diagnosed, the type of treatment is not immediately evident. Depending on the size of the tumour and possible spread to the lymph nodes, neoadjuvant systemic therapy is recommended prior to surgery. Neoadjuvant therapy is the treatment given prior to the main treatment, where systemic therapy is a treatment reaching and affecting cells all over the body according to the dictionary on the website of the National Cancer Institute (http://www.cancer.gov/). In general, surgery is applied in the presence of a small tumour (< 2 cm) without spread to the lymph nodes. Neoadjuvant systemic therapy is appropriate for large tumours (≥ 2 cm) or when spread to the lymph nodes is detected. The primary objective of neoadjuvant systemic therapy is to decrease the size of the tumour (which makes surgery less complicated and a less radical procedure). For neoadjuvant systemic therapies, hormonal therapy and chemotherapy are used in AVL. Dosing neoadjuvant chemotherapy yields knowledge of the applicability of certain adjuvant chemotherapies. In other words, the response to a neoadjuvant chemotherapy type indicates whether the same chemotherapy type will be useful after surgery. While receiving chemotherapy depends on the age of the patient, hormonal therapy is only received in the presence of hormone receptors in the tumour. The existence of these receptors indicate the sensitivity of the tumour to hormones. If the pathological results show that the tumour is resistant to hormones, hormonal therapy will not be proposed. This thesis focuses on the breast cancer patients assigned to the neoadjuvant chemotherapy care pathway (highlighted in Figure 1).

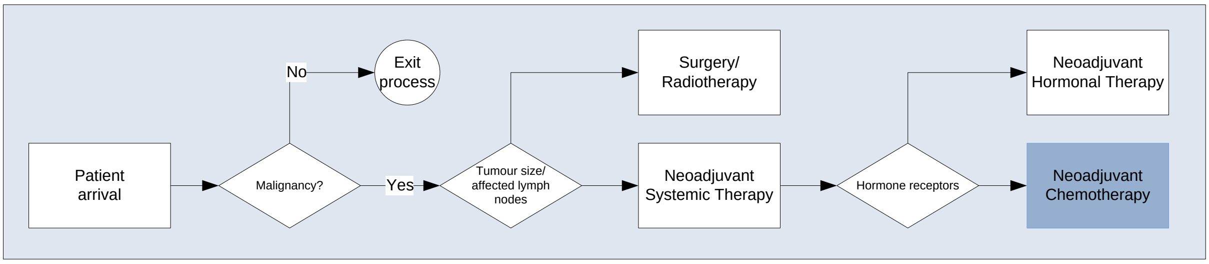

Figure 1: Process of establishment of a treatment plan with neoadjuvant chemotherapy

Once patients are assigned to the neoadjuvant chemotherapy care pathway (CP), additional tests and pre-assessments are required prior to the chemotherapy treatment. These examinations are vital to obtain information necessary to select the best applicable treatment plan. They serve to determine relevant characteristics of the tumour, detect possible metastases and ascertain the physical condition of the patient. During this phase, several appointments are scheduled at different departments. In general, over ten appointments are required to be scheduled to make an MRI (magnetic resonance imaging) scan, an X-ray of the lungs and an electrocardiography (ECG) for example. These appointments come with a number of scheduling constraints (e.g. related to radioactivity or sequencing). In addition, this set of appointments varies between patients. This irregularity is due to different patient flows, patient preferences, available examination reports and other conditions. Chapter 2 discussed the appointments and their applicability in more detail.

When all required examinations are performed and the definitive treatment plan is established, the chemotherapy treatment is dosed. Once all chemotherapy treatments are received (over a period of several months), this phase terminates whereupon an MRI scan enables the response measurement. Hereafter, preparations for surgery take place.

1.3 Problem identification

Once malignancy is determined, patients desire in general to be treated as quickly as possible. Since the tests and pre-assessments do not form a part of the treatment (i.e. they are not directly contributable to reduction or removal of the tumour or tumours), the throughput time of this phase is requested to be as small as possible. Aside from the fact that a tumour is continuously growing and therefore desired to be treated as quick as possible, patients are in a period of uncertainty after the diagnosis. The characteristics of the tumour and possible spread to other parts of the body are yet to be determined. Regarding the throughput time from the assignment of the patient to the neoadjuvant chemotherapy CP until the first chemotherapy treatment, a maximum time span of two weeks is desirable, according to the management. Even though the process is not transparent and therefore little evidence is available, management suspects that a minor part of the patients satisfy this aspiration. This forms the primary problem of this thesis.

While for the CP it is known which appointments patients usually have (i.e. standard appointment) and the approximated duration of each appointment, it is unknown how much capacity this patient group requires. Fluctuating patient arrivals in combination with deviations from the CP makes it difficult to determine the required capacity. These deviations are for example caused by inequalities in the performed medical examinations or different chemotherapy types. These are, in turn, induced by differences in tumour characteristics, physical condition, patient preferences and other issues. Knowledge about the future required capacities is desired. As discussed in Section 1.1, it is expected that the number of patients increases in the upcoming years. What the impact of this change will be on the required capacity is unknown. Where the primary problem is focused on the CP until the first chemotherapy treatments, this secondary problem comprises the entire CP.

Conclusion

To summarise, the primary and secondary problem of this study are:

- The throughput time from the moment a patient is assigned to the neoadjuvant chemotherapy care pathway until the first chemotherapy treatment is unknown and perceived to be too long.
- Future required capacities are unknown.

1.4 Research objective and research questions

This section introduces the research objective of this study. In order to achieve the objective six research questions are defined. They are briefly discussed to create a structured research approach.

Research objective

To assess the capacity required for a throughput time of two weeks, from the assignment of patients to the neoadjuvant chemotherapy care pathway until the first chemotherapy treatment, and to determine future required capacity.

Research questions

1. What is known about hospital decision making in resource capacity planning and control?

Chapter 2 comprises a literature study in OR/MS methods for planning decisions. Literature on different planning problems is listed and the usability of each method is discussed.

2. What is the treatment regimen of the care pathway for breast cancer patients prior to neoadjuvant chemotherapy?

Chapter 3 sets forth a comprehensive process description, based on interviews, observations and documents related to the care pathway where the focus lays on the part until the first chemotherapy treatment. The planning and control of the process are discussed in Section 3.2.

3. What is the current performance of the care pathway, according to indicators from a logistical point of view?

In order to improve the process, we need to know the current performance. Section 3.3 describes the indicators used to measure the performance of the CP. Data analysis is the first step in quantifying the current situation and enables to detect bottlenecks in the process. The problem analysis is discussed in section 3.4.

4. Which approach is required to reach the objective of this study?

A combination of two methods is selected to reach the objective. Chapter 4 describes the first method as an approximation model and reports the results. The second method, that serves to reach the objective of this research, is discussed in Chapter 5.

5. What is the effect time slot allocation on the throughput time from the assignment to the care pathway until the first chemotherapy treatment?

The improvement of planning decisions is covered in research question 5. The computational results of the chosen modifications in planning decisions are reported in Chapter 6. This addresses the primary problem of this study.

6. What are the required capacities for different arrival scenarios?

For a number of arrival scenarios, the model presented in Chapter 5 simulates the required capacity. Chapter 6 also presents the computational results for the secondary problem of this study.

1.5 Scope

This study is restricted to the process from the assignment to the neoadjuvant chemotherapy CP of breast cancer patients until the evaluation MRI scan after all chemotherapy treatments. Internal processes like pathology and pharmaceutical operations for chemotherapy are considered as fixed. These processes can be relevant for the observed process but interventions in these processes are outside the scope of this study. Appointments during the CP that are not related to the chemotherapy treatment are excluded from this study as well (i.e. radiotherapy consults, heredity examinations, physiotherapy and preparation for surgery).

The set of appointments with the associated restrictions (caused by medical grounds) that is required in the current process is assumed to be appropriate. That is, the necessity of appointments will not be questioned. Only when explicitly referred to an appointment as exchangeable or not strictly necessary, the inclusion in the set of appointments can be discussed. Since the duration of appointments is a study in itself, we suppose the duration of the appointments to be equal to the scheduled duration of appointments unless there are reasons to assume otherwise.

Financial aspects are not considered in this study. The financial consequences of modifications in planning decisions will not be discussed. Furthermore, patient satisfaction is not considered as the focus is on logistical features such as throughput times and capacities.

We use the framework of Hans, Van Woudenhoven and Hulshof (2011), in order to indicate the hierarchical nature of decision making in this study. The horizontal axis indicates the various managerial areas and on the vertical axis the hierarchical levels are shown. We focus on tactical planning decisions (highlighted in Figure 2). Strategic and operational decisions are outside the scope of this study. We consider the strategic planning decisions to be adequate (e.g. the capacity is not required to be enlarged and current patient routing is appropriate). Operational planning decisions improve current performance but will not reach the objective of this thesis.

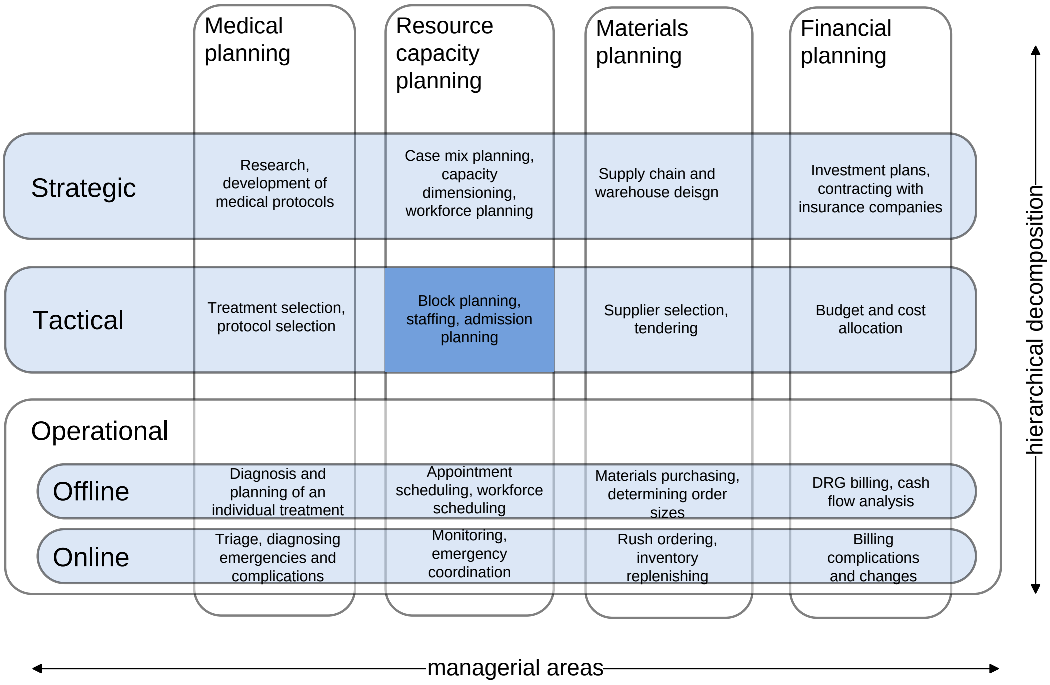

Figure 2: Framework for health care planning and control (general hospital). Hans et al. (2011)

2 Literature review

In this chapter we review literature to determine appropriate planning decisions to reach the objective and techniques to elaborate the planning decisions. In section 2.1, Operations Research and Management Science (OR/MS) methods for decision making in resource capacity planning and control are discussed to determine the most suitable method(s) for this study. Section 2.2 gives the conclusion of the literature study.

2.1 OR/MS methods for hospital planning decisions

In order to study a system, Law (2007) distinguishes analytical solution and simulation as forms of mathematical models. Hulshof et al. (2012) compose a more comprehensive overview of OR/MS methods, useful for planning decisions in healthcare (Hulshof, Kortbeek, Boucherie, Hans, & Bakker, 2012). They differentiate mathematical programming, Markov processes, queuing processes, computer simulation and (meta)heuristics. Applications of aforementioned techniques on tactical planning decisions are discussed by means of literature in order to find the best method(s) to reach the objective of this research.

2.1.1 Mathematical programming

According to Berry (2013), mathematical programming involves building an abstract model of a real-world situation or system in some formal language. Kuip (1993) includes solution variables, constraints and an objective criterion. It involves decision making situations in which a good or optimal decision must be reached.

Du, Jiang, Yao and Diao (2013) focus on optimising the scheduling of CPs. They present a mathematical model of the scheduling problem which minimises the total completion time of all patients. A hybrid genetic algorithm is proposed. The sequence of actions is considered as fixed and the available capacities are input variables.

Several studies (Kwak & Lee, 1997; Smith, Jr, Hansen, Golladay, & Davenport, 1976) use linear programming (LP) to determine staffing levels. Kwak and Lee (1997) use LP to allocate human resources over different departments (Emergency, Radiology and Nuclear Medicine). Budget allocation is used to limit the total amount for payroll. Smith et al. (1976) present an application of mixed integer linear programming to determine the optimal staff level. They try to minimise the cost of staffing and include the effect of scale and patient mix. Blake and Donald (2002) use integer programming (IP) for the assignment of OR time to five surgical divisions. The schedule produced by the IP model is improved by means of a heuristic. The objective function is to minimise the undersupply of operating room time.

Mathematical programming is very useful to allocate resources and incorporate static care pathway. An objective function is minimised or maximised.

2.1.2 Markov processes

White and White (1989) define the key characteristic of Markov processes as the transition probability from the current state of the process to the state of the process at the next decision epoch depends only on the current state and not on earlier states and actions of the process. This is known as the memoryless property.

Kolisch and Sickinger (2008) use a Markov Decision Process (MDP) to model the problem of allocating available resources dynamically to patient groups. Different decision rules and types of appointment schedules are evaluated. Nunes, De Carvalho and Rodrigues (2009) model the control of patients' admission as an MDP. At the beginning of each period, the system state is observed and a decision is made about the number of new patients that must be admitted from each specialty in the next period. Thus, a sequential decision problem is formed with the Markovian property.

McClean and Millard (1998) model the patient flows in a geriatric department through a Markov model including acute care, rehabilitation and long-stay care. They attribute cost to staying in each state and determine the expected costs for different models. A similar approach is used by Kapadia, Vineberg and Rossi (1985), to model the flow of patients through a rehabilitation hospital. The emphasis is on tracing the treatment patterns patients experience, which they describe as a sequence of treatments of one week (e.g. surgery and rehabilitation).

The discussed articles all include stochastic probabilities for the transition of one state to another where decisions are independent on historical events (i.e. memoryless property). Each period is equally long in which one treatment is received.

2.1.3 Queuing processes

A queuing system is described by Gross, Shortle, Thompson and Harris (2008) as customers arriving for service, waiting for service if it is not immediate, and if having waited for service, leaving the system after being served. Hall (2006) gives a more scientific description and defines a queuing model as a mathematical description of a queuing system which makes some specific assumptions about the probabilistic nature of the arrival and service process, the number and type of servers, and the queue discipline and organisation. An example of a queuing model is shown in Figure 3.

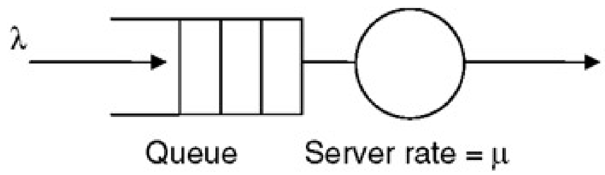

Figure 3: Queuing node with customers arriving with rate λ and a single server with server rate μ

For individual appointments, Thomas, Williams, Burnet and Baker (2001) calculate the capacity required to attain a predetermined service level (with patient arrivals according to a Poisson distribution) by means of queuing theory. The service level is regarded as the percentage of patients which is served within a specified time period.

Besides for single appointment types, queuing theory is used for (parts of) CPs. Patient flow networks resemble queuing networks. Côté (2000) states that queuing performance measures such as time in the system and traffic intensity have direct correspondence to the patient flow characteristics. Several studies (Maridah & Basri, 2013; Filipowicz & Kwiencien, 2008; Jiang & Giachetti, 2008; Liyanage & Gale, 1995) consider hospital departments as queuing networks. Maridah and Basri (2013) use an open queuing network to model the Outpatient Clinic (OC). They characterise the use of queuing theory in three parts: (a) arrivals or input, (b) queuing discipline and (c) the service facility. Jiang and Giachetti (2008) model the outpatient facility as a multi-class open queuing network. A simulation model is created to evaluate the accuracy of the model. Filipowicz and Kwiecien (2008) discuss queuing systems and networks. They include the application of a model of chemotherapy unit. The chemotherapy unit is presented as a closed BCMP network with routing probabilities. A BCMP network is a class of queuing network for which a product-form equilibrium distribution exists. Liyanage and Gale (1995) present a study in which the available resources of the emergency facility are optimised. This is done through the combination of queuing and simulation. Thereafter, a simulation model is used to find the optimal number of servers of the system.

In the discussed articles, either queues are analysed individually or in a network. With single queuing nodes, performance of single appointment types can be determined. Networks are required to analyse (a part of) a CP which include defined interrelations between the different appointment types (e.g. routing matrix). The networks are particularly appropriate for same day appointments.

2.1.4 Computer simulation

In a simulation, a computer is used to evaluate a model numerically, and data are gathered in order to estimate the desired true characteristics of the model (Law, 2007). As this description suggests, computer simulation is a powerful tool to analyse the performance of a system. Law classifies simulation models along three dimensions: static vs. dynamic, deterministic vs. stochastic and continuous vs. discrete. Dynamic, stochastic and discrete simulation models are called discrete-event simulation models which applies to the process of patient routes.

Benneyan (1997) discusses a case study concerning the paediatric department. The number of staff and appointment durations are decision variables in the proposed simulation model. Performance measures are, among others, patient waiting times and resource utilisation. He concludes that stochastic methods are important to use in patient arrivals to incorporate the process variability. Furthermore, Cardoen and Demeulemeester (2007) evaluate care pathways through a generic discrete-event simulation model. A number of settings is evaluated and compared for two case studies.

Brenner et al. (2009) analyse the emergency department (ED) through a simulation study. The performance of the current configuration of staffing level and equipment resources is validated using the average throughput from the data. Modified configurations are simulated to measure the results of increased or decreased staffing or equipment resources. The optimal number of nurses, doctors and testing equipments are separately determined based on patient throughput, resource utilisation, time in waiting room and time in ED. Zeng, Ma, Hu, Li and Bryant (2012) performed similar study to improve the quality of care in the ED of a hospital. Different configurations are tested (additional nurses and a additional CT scanner) which appears to result in improved length of stay and reduced waiting times.

Azari-Rad, Yontef, Aleman and Urbach (2014) present a discrete event simulation study to model the perioperative process. The process starts with admission to the hospital and ends when patients are discharged. The performance of the system is measured by the mean number of surgical cancellations. Scenarios as surgeons' surgical block assignment and patient scheduling rules are simulated including combinations with additional ward beds.

In the examined articles, simulation studies were performed to determine the performance of certain settings such as the staffing level or equipment resources. In all articles, different configurations are simulated to determine the performance in each situation.

2.1.5 (Meta)heuristics

According to Olafsson (2006), the metaheuristic approach to problem solving is to start by obtaining an initial solution or an initial set of solutions, and then initiating an improving search guided by certain principles. In each step of the search algorithm, there is always a solution (or a set of solutions), which represents the current state of the algorithm.

Vermeulen et al. (2009) present an adaptive approach to automatic optimisation of a resource calendar. They describe a model for scheduling multiple patient groups to a single CT scanner. Heuristics are proposed to schedule the patients and to adjust the capacity between patient groups dynamically.

(Meta)heuristics can be applied to heuristically determine a good solution to a planning problem. Starting with an initial solution, several methods can be used to iteratively improve the performance.

2.2 Conclusion

In literature, applications of queuing and simulation are commonly used methods for improvement of healthcare processes. The Outpatient Clinic and Emergency Department are frequent subjects of research. In order to determine the most suitable method or methods to achieve the objective of this study, we analyse the mentioned techniques.

As the performance of the process highly depends on the sequence of different appointments, we require the model to be able to deal with flexible routing. This should not be fixed nor based on a static routing matrix. Dynamic appointment planning is very hard, if not impossible to incorporate in mathematical programming. In the CP, appointment planning is dependent on the availability of resources in future. While future decisions depend on past decisions in our process, MDPs are not suitable. Heuristics can be applied to create an initial solution and improve the solution iteratively through specified rules. However, this method is mainly suitable to allocate capacity of fixed size.

Queuing theory is highly suitable for walk-in processes, but less appropriate for appointment planning. For individual appointments, queuing theory is proven to be useful. Routing between nodes should be defined with queuing while this is dynamic in the CP prior to the chemotherapy treatments. The level in which constraints can be included in a queuing model is limited. Simulation can be used to simulate configurations and evaluate the performance of the process. Jacobson, Hall and Swisher (2006) state that "an important advantage of using discrete-event simulation, over other modelling techniques like linear programming or Markov chain analysis, when modelling a health care clinic is the capacity to model complex patient flows through health care clinics, and to play "what if" games by changing the patient flow rules and policies" (p. 213). Analysing "what if' situations fits perfect with different arrival scenarios.

To conclude, a combination of queuing theory and computer simulation forms the most appropriate method for this study. The deficiencies of both methods are resolved through the conjunction; a queuing model is limited to approximate the required capacities, while a simulation model requires an initial configuration. The approximation from the queuing model can be used as initial configuration for the simulation model. Subsequently, the initial configuration is modified to determine appropriate solutions. The next chapter describes the context analysis from which we deduce both models.

3 Context analysis

Section 3.1 describes the process analysed in this study. Section 3.2 discusses the planning and control of the process. Section 3.3 gives the current performance of the current situation. The problems are analysed in section 3.4. Section 3.5 forms the conclusion of this chapters.

3.1 Process description

This section describes the neoadjuvant chemotherapy CP in detail. Frameworks of CPs are used in order to structure the process. They are merged into a single framework, as shown in Figure 4 (Hummel, Otter, & de Vries, 2010; Breast Cancer: Dutch Guideline, 2012; van Vliet, Sermeus, van Gaalen, Sol, & Vissers, 2010). With the aid of this general framework, the framework suitable for this study is generated.

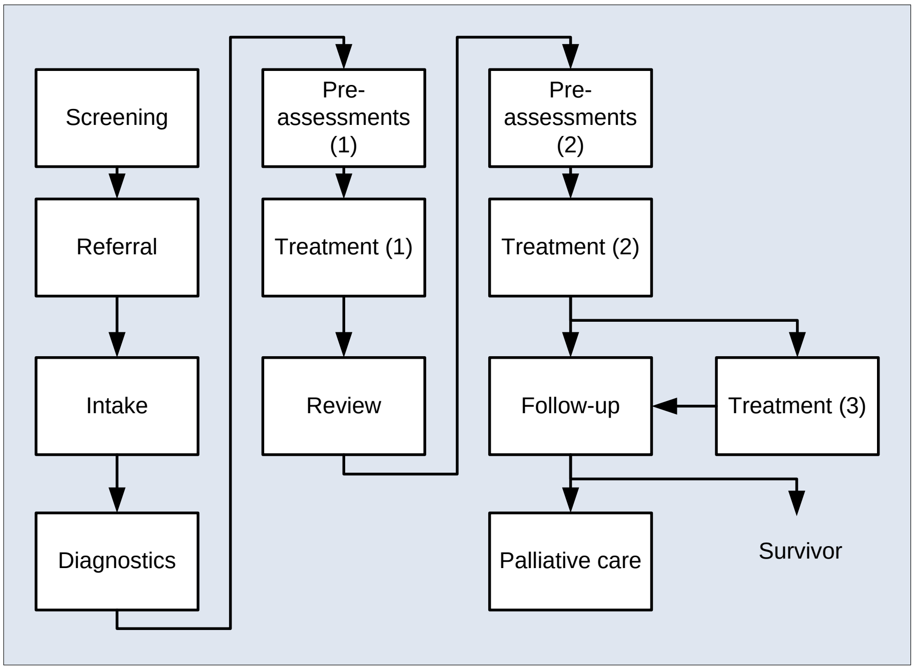

Figure 4: Entire CP of patients for whom treatment (1) is neoadjuvant chemotherapy

As this study focuses on the CP of neoadjuvant chemotherapy patients, several segments of Figure 4 are omitted. Figure 5 on the next page is a deduction from the general framework and shows the position of the neoadjuvant chemotherapy CP. We discern three phases in the CP:

1. Additional tests and pre-assessments

2. Neoadjuvant chemotherapy treatment

3. MRI scan

The focus of this study is on the first phase as the main problem concerns the throughput time from the assignment to the CP until the first chemotherapy treatment. Both other phases are briefly discussed in the following paragraphs.

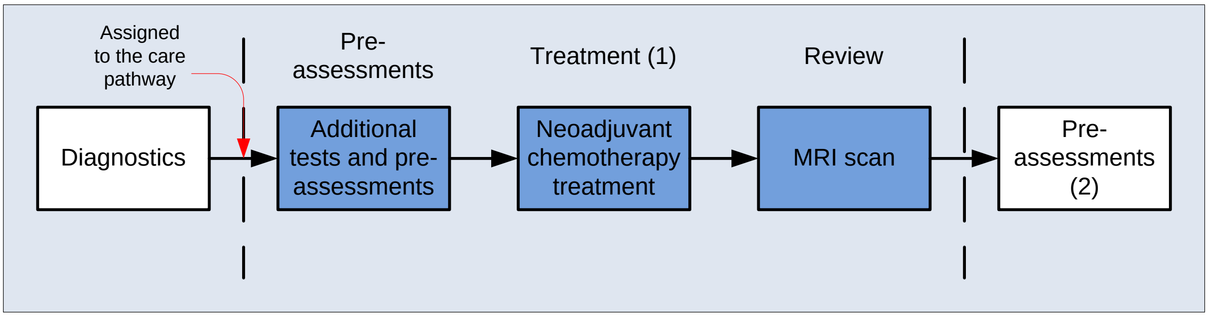

Figure 5: Positioning neoadjuvant chemotherapy in the entire care pathway (involved segments highlighted)

3.1.1 Additional tests and pre-assessments phase

The additional tests and pre-assessments phase (abbreviated to ATP) consists of (1) a preliminary appointment with a nurse practitioner, (2) tests and pre-assessments, (3) an appointment with an internist and (4) a consult at the outpatient clinic to prepare patients for the chemotherapy treatments, as shown in Figure 6. We refer to 'additional' since a number of tests is already performed to reach diagnosis.

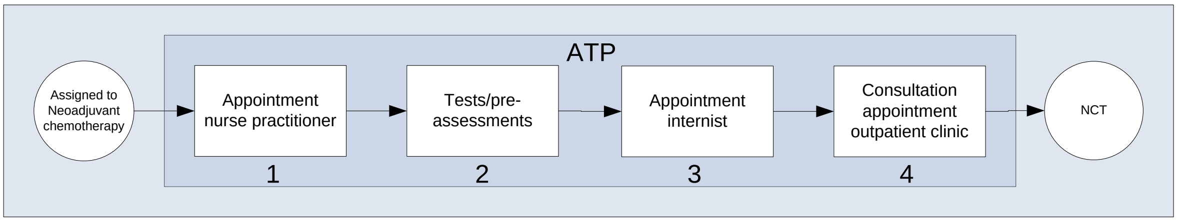

Figure 6: Additional tests and pre-assessments phase

1. Appointment with a nurse practitioner

Diagnosis is formed during the multidisciplinary team deliberation. Since patients are not present at the moment they are assigned to the CP, an appointment with an nurse practitioner (abbreviated to NP) is required to inform patients about the proposed treatment plan.

2. Tests and pre-assessments

A number of tests and pre-assessments is required to take place prior to chemotherapy treatment. Tests are required to create a complete view of the tumour and possible spread to other parts of the body. Pre-assessments chart the physical condition of patients and identify whether patients are 'healthy' enough for chemotherapy treatments. The tests and pre-assessments of this phase are listed in Appendix A. A second appointment with the NP is scheduled in order to obtain the anamnesis. Some patients receive the Sentinel Node Procedure (SNP). This is a surgical procedure in which lymph nodes are removed.

3. Appointment with an internist

When all tests and pre-assessments are performed and the pathological results are reported, an internist discusses the outcomes of the examinations and announces the chemotherapy type that will be dosed.

4. Consultation appointment outpatient clinic

Patients are informed about the treatments at the outpatient clinic. A nurse informs and prepares patients (mentally) for the chemotherapy regimens.

3.1.2 Neoadjuvant chemotherapy treatment phase

The neoadjuvant chemotherapy treatment phase (abbreviated to NCT) commences once the ATP phase is completed. This phase consists of a number of treatments. For each chemotherapy treatment, patients stay in the hospital for a certain period of time in which intravenous therapy is used. The intermediate response to the chemotherapy is evaluated by means of an MRI scan and discussed during an appointment with an internist. Subsequently, patients continue with either the same chemotherapy type or a different type, depending on the response.

3.1.3 Review phase

After all required treatments are dosed during the NCT phase, another MRI scan displays the effect of the chemotherapy treatments for the second time. Although this appointment is considered as part of the CP, the discussion of the results is not. This is generally done by the surgeon during an appointment in which the surgeon previews the surgery.

The process included in this study is shown in Figure 7. It represents the tripartite division of the CP with the additional tests and pre-assessments phase (ATP), the neoadjuvant chemotherapy treatment phase (NCT) and the Review phase.

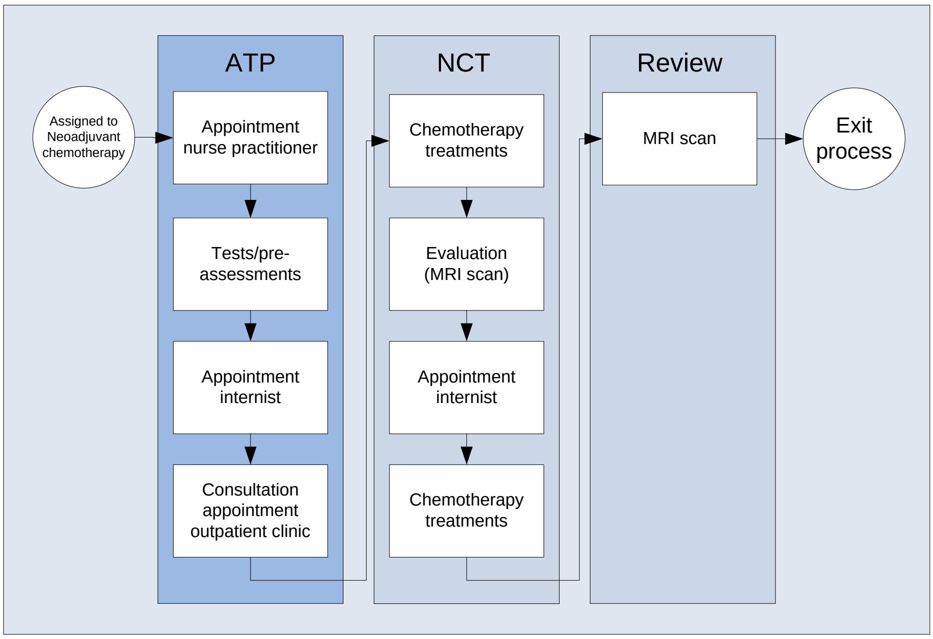

Figure 7: Research process (ATP phase, NCT phase and Review phase)

3.2 Planning and control

This section discusses the planning and control of the process. Paragraph 3.2.1 describes the planning and control with regard to the ATP phase. The chemotherapy treatment and review are briefly discussed in paragraph 3.2.2.

3.2.1 Additional tests and pre-assessments

During the first appointment with the NP, the applicability of each (of the remaining) standard appointments is assessed. Then, the required appointments are planned. Both patients' agendas and the agendas of the involved entities are stored in the hospital information system. Patients are sequentially planned.

Although a single planner is committed to the planning of the appointments, planning authority is dispersed over departments. Appointments at the Radiology department, Nuclear Medicine department and the Outpatient Clinic are planned by their own staff. The planner applies for a desired date (and possibly time), but she does not has the authority to plan the appointment. This is also true for biopsy, ultrasonography and the MRI scan, although time slots are applied. For the other appointments, capacity is shared with other patient groups. Appointments cannot be planned without the consideration of radioactive materials and sequencing. The planner must follow guidelines regarding appointment planning. These restrictions are not embedded in the software.

While for most tests and pre-assessments the outcomes are known within minutes after the appointment, the results of the biopsy take longer to be reported. This is mainly due to the establishment of the presence of the protein called HER2/neu in the breast tissue. Two other relevant receptors are the oestrogen receptor (ER) and the progesterone receptor (PR). This information is of crucial importance for the type of chemotherapy dosed. The pathological results are required to be reported prior to the appointment with the internist. While an appointment with the internist is being planned in advance, the time to finish the report fluctuates. To ensure that the results are reported at the time of the planned appointment with the internist, a minimum of ten days is applied between the biopsy appointment and the appointment with the internist.

When the results of the biopsy show that all three receptors (HER2/neu, ER and PR) are absent and the imaging results indicate spread to the sentinel lymph nodes, the sentinel node procedure (abbreviated to SNP) is performed. Patients with at least one chemotherapy treatment and no SNP are referred to as regular patients and patients with at least one chemotherapy treatment and SNP as SNP patients.

3.2.2 Treatments and review

Different types of chemotherapy are used in AVL. Each type requires its own schedule with varying number of treatments and time intervals in between. Besides treatments, appointments with an NP, an MRI scan and an appointment with an internist is required. The review phase is limited to an MRI scan. For more details, see Appendix B.

3.3 Performance indicators

For both problems stated in Section 1.3, we need to chart the current performance of the process. When the current performance is unknown, improvement is impossible to measure. To select the performance indicators suitable for the research process, we use the tool proposed by Vanhaecht and Sermeus (2003). They define five domains in the Leuven Clinical Pathway Compass which include indicators of a CP: clinical, service, team, process and financial indicators. Our focus is on process indicators (highlighted in Figure 8).

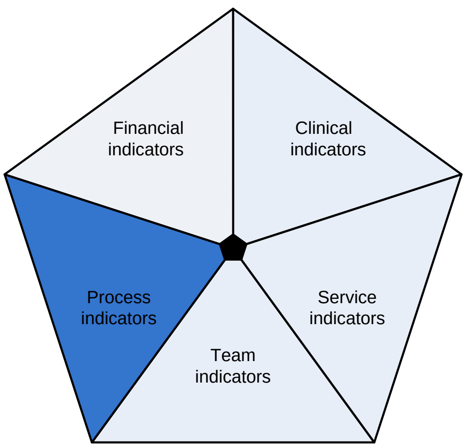

Figure 8: Leuven Clinical Pathway Compass. Vanhaecht and Sermeus (2003)

Clinical indicators are excluded since they are directly related to the disease and the impact of the disease. Clinical indicators such as pain measurement are irrelevant. Service indicators show patient satisfaction which is outside the scope of this research. Team performance depends on the planning and control of the CP. Team indicators are for example relational coordination and team satisfaction but are not included in this study.

The focus of this study is on process performance and thus on process indicators. Vanhaecht and Sermeus (2003) refer to process throughput time as one of the most important process indicators. In addition, waiting times and the sequencing of key interventions are mentioned. Although costs are not included in this research, the number of appointments per patient such as MRI scans or consults by an NP can be used as a proxy for cost. The same applies for the length of stay. In order to indicate the capacity required for this group of patients, the number of appointments is necessary to be identified.

3.3.1 Throughput time

Indicator 1: Throughput time between the moment a regular patient is assigned to the neoadjuvant chemotherapy CP and the first chemotherapy treatment (in days)

Figure 9 shows the results of this indicator. Patients started in 2013 received the first chemotherapy treatment with a slightly decreased throughput time, compared to patients started in 2012. As was presumed by management (Section 1.3), the desired service level of 90% of the regular patients served within 14 days is not achieved. Although the performance is improved in 2013, the current performance significantly deviates from the desired situation as 90% of the patients receive service within 28 days (Table 1).

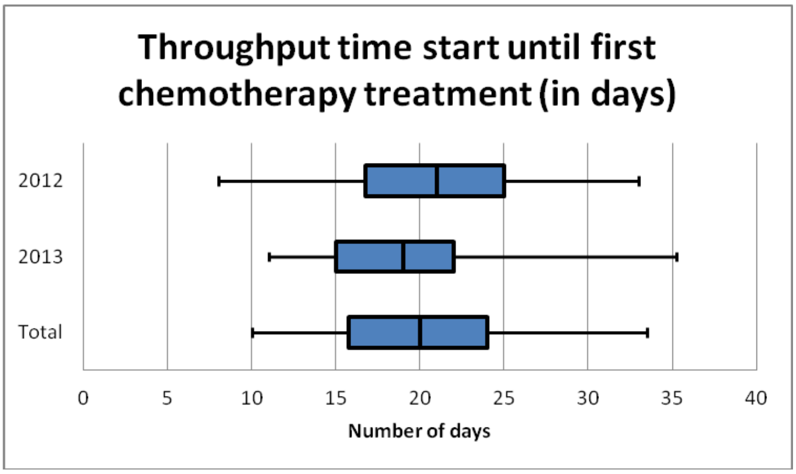

Figure 9: Throughput time between the moment a patients is assigned to neoadjuvant chemotherapy treatment until the first chemotherapy treatment (patients assigned to the care pathway in 2012 and 2013 until 9-12-2013; with N = 296 patients [2012: n = 140, 2013: n = 156]; the ends of the whiskers represent the 5th and the 95th percentile)

Table 1: Percentage of patients served with a throughput time within two and three weeks (patients assigned to the care pathway in 2012 and 2013 until 9-12-2013; with N = 296 patients [2012: n = 140, 2013: n = 156])

	Average throughput time (in days)	Standard deviation (in days)	% observed throughput times ≤ 14 days	% observed throughput times ≤ 21 days	90 % of throughput times ≤ number of days
2012	20.57	7.04	16%	57%	29
2013	19.78	6.87	21%	69%	28
Total	20.15	6.95	19%	63%	29

3.3.2 Waiting time

Indicator 2: Throughput time between the moment a patient is assigned to the neoadjuvant chemotherapy care pathway and the appointment date (in days)

Waiting times are useful indicators as they identify possible bottlenecks in the CP. Unfortunately, since appointment times are dependent on each other, the observed waiting times do not truly reflect the availability of the capacity. However, these throughput times are useful to identify bottlenecks as they indicate access times. Therefore, we include this indicator for all appointments in the ATP phase. The Sentinel Node Procedure is included since this procedure pertains a significant part of the patients and influences the course of the remaining CP. All appointments are given in Appendix A. The box plots are shown in Figure 10.

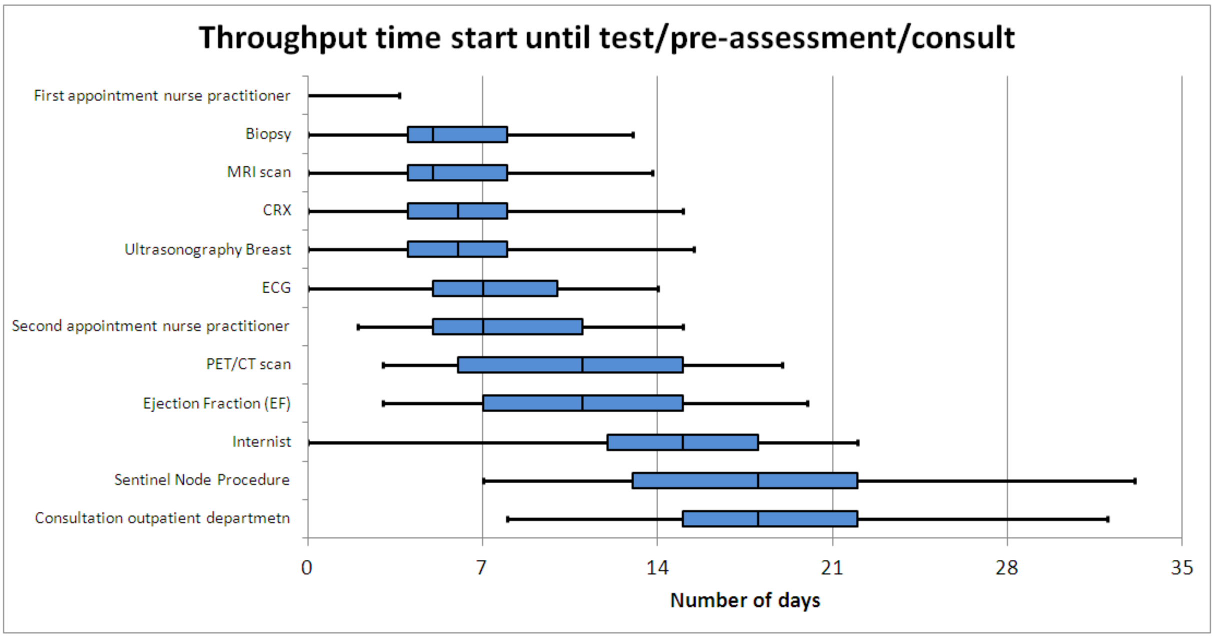

Figure 10: Throughput time between the moment a patient is assigned to the neoadjuvant chemotherapy care pathway until a certain test, pre-assessment or consult (patients assigned to the care pathway in 2012

and 2013 until 9-12-2013; with N = 330 patients [2012: n = 155, 2013: n = 175]; the ends of the whiskers represent the 5th and the 95th percentile)

For all appointments, except for the first appointment with the NP, great variety in throughput times is shown, indicating irregular performance of individual appointments. Figure 10 corresponds with the semi-fixed sequence of appointments (described in section 3.1.1). Regarding the examinations, long throughput times are measured for the EF and the PET/CT (positron emission tomography – computed tomography) scan. The large width of these box plots suggests varying availability of capacity. This is partly attributable to downtime of machines but also due to fluctuating demand of other patient groups. Figure 11 shows the fluctuating number of days between the input date of an appointment and the appointment date, corresponding with the large width of the box plots. The waiting time for the appointment with an internist is repeatedly over 14 days, making it unable to start with treatment within two weeks. See Appendix B for detailed performance on waiting times.

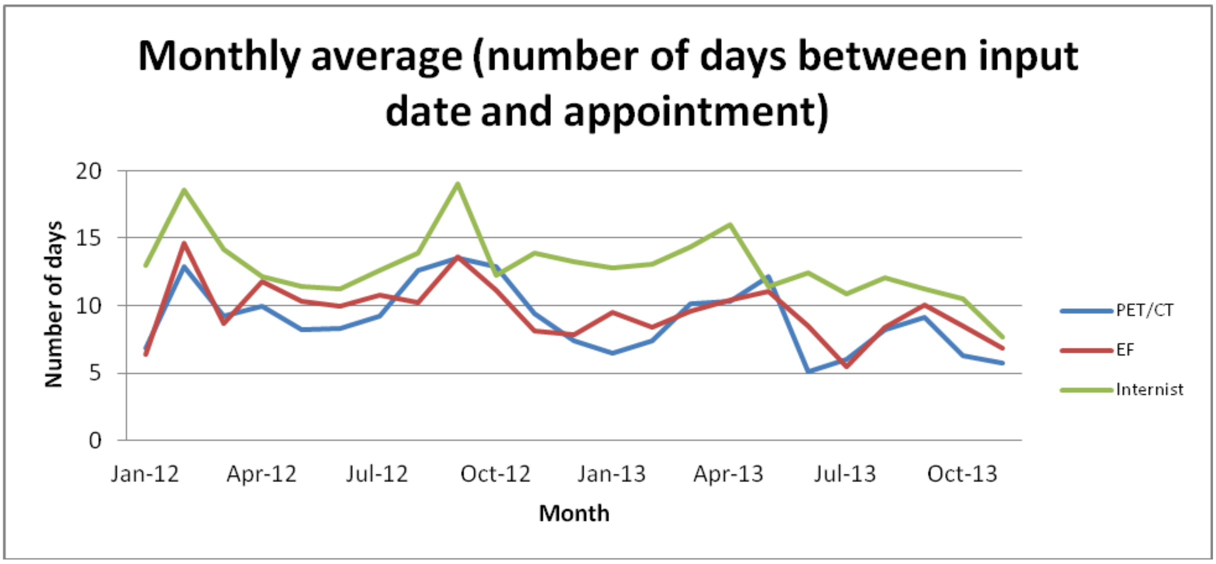

Figure 11: Monthly average number of days between the input date and the appointment date of PET/CT, EF and internist (from data analysis)

3.3.3 Appointment probability

Indicator 3: Probability that an arbitrary patient requires the appointment

To determine the required capacity, we assume that each appointment in the CP occurs once or not at all. It may happen that an appointment type is scheduled more than once, but these do not form a part of the standard CP and are therefore outside the scope of this study. Although a standard set of appointments is used, the applicability varies. For some patients, specific tests or pre-assessments are redundant or inappropriate, e.g. patients who are already seen at another hospital. Some examinations may already be performed prior to the appointment with the NP.

Results are shown in Table 2. This is the same list of appointments that is used for indicator 2, complemented with the first chemotherapy treatment.

Table 2: Probability Pi of the occurrence of appointment type i (data obtained from 01-01-2012 until 09-12-2013 for patients who received ≥ 1 chemotherapy treatment and/or terminated the process with N = 330 patients [2012: n = 155, 2013: n =175])

Appointment type	Probability P_i: appointment i is requested for an arbitrary patient
1. First appointment NP	95%
2. Biopsy	61%
3. MRI scan	82%
4. ECG	86%
5. PET/CT scan	82%
6. EF	92%
7. Ultrasonography Breast	80%
8. CRX	80%
9. Second appointment NP	82%
10. SNP	18%
11. Internist	87%
12. Consult outpatient clinic	85%
13. 1st Chemotherapy treatment	91%

Table 2 shows that although the listed appointments are included in the ‘standard’ CP, the realised probabilities significantly deviate from 100%. The presence of patients who prematurely exit the CP contributes to this. The relatively low probability for biopsy is due to, among others, retrieval from other hospitals and examinations prior to the start date. Results from other hospitals lower other appointment probabilities as well. As said before, the SNP is not included in the list of standard appointments and thus deviates from the other appointments.

3.3.4 Conclusion

The desired service level is not achieved. Instead of 14 days, 90% of the patients received chemotherapy treatment within 29 and 28 days, respectively, in 2012 and 2013. When analysing the waiting times for appointments, long waiting times for appointments are observed at the Nuclear Medicine department and for the appointment with the internist. This suggests that insufficient capacity is available when required. The standard set of appointments appears to significantly derogates from being standard for all patients.

3.4 *Problem analysis*

The two problems introduced in Section 1.3 are more thoroughly discussed in this section.

3.4.1 Throughput time

Data analysis shows that the throughput time from the assignment to the CP until the first chemotherapy treatment is too long (Figure 12).

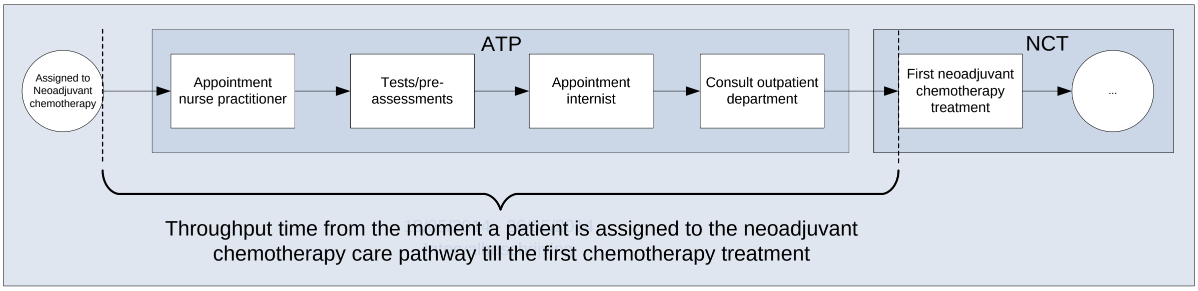

Figure 12: Main problem

As interviews with staff clarify and the data analysis shows, capacity is often not available when required. This forms the main cause inducing long throughput times. For appointments at the Nuclear Medicine department, the constructed box plots show wide ranges (Figure 10). This corresponds with the varying capacity that is available for this group of patients as the demand (of other patient groups) varies. This is caused by, among others, ongoing studies which require numerous appointments at the PET/CT scan and EF.

For the appointment with the internist, the desired date is close to the lower bound of ten days after the biopsy appointment. If we analyse the throughput times (see Appendix C), we see that a quarter of the patients had a time period of at least 13 days between the two appointments. This suggests that capacity for internist appointments is not available at the desired moments. Since other appointments may have caused the appointment with the internist to be scheduled after the ten days after the biopsy, we cannot attribute the entire delay in appointment to waiting time for the internist appointment. New agreements with the Pathology department include a period of five workdays in which the pathology results are reported.

3.4.2 Requested capacity

The capacity used by this patient group is not known. Not for a single appointment type, the utilised capacity is recorded. Since it is not known what the current requested capacity is, future required capacity is also unknown. The required capacity is referred to as the number of appointments necessary to serve all neoadjuvant chemotherapy patients. Hospital-wide growth rates in patient numbers are determined but not specifically for this patient group.

3.4.3 Conclusion

From the problem analysis we deduce two main problems:

1. The throughput time from the assignment to the neoadjuvant chemotherapy care pathway until the first neoadjuvant chemotherapy treatment is currently 28 days and is required to be 14 days (for at least 90% of the regular patients)

2. The future required capacity for this patient group is unknown.

3.5 Approach

The objective of this research consist of two goals. The primary goal of this study is to determine time slot configurations which meet the required patient service level in the most efficient way. A configuration is defined as the number of time slots assigned to each appointment type. The service level is regarded as the percentage of patients receiving their first chemotherapy treatment within 14 days and is set to 90%. The most efficient way refers to the highest utilisation. The secondary goal is to provide an indication of the capacity that is required for future demand for all appointments in the CP. For appointments subsequent to the first chemotherapy treatments, time slots are not included.

To determine the required capacity for future patient arrivals, a number of scenarios is defined. The manager approximates the annually growth of patient arrivals to be 5-10%. Therefore, we include both scenarios where the arrivals are 5% and 10% higher than in the current situation. In addition, we consider the situations when patient arrivals are increased with 20% and 50%. This corresponds to the long-term expectations of growth in patient numbers described in Chapter 1. A scenario with less arrivals than in the period 2012-2013 is also included to analyse the consequences of a declined arrival rate (Table 3). For all scenarios, the defined arrival rate is static for the entire period.

Table 3: Future arrival scenarios

Scenario	Arrival rate
Base scenario	Current arrival rate
Scenario 1	+ 5%
Scenario 2	+ 10%
Scenario 3	+ 20%
Scenario 4	+ 50%
Scenario 5	- 20%

A combination of queuing theory and simulation is used to reach both goals. By means of queuing theory, required capacities for appointments related to the main problem of this research are approximated, through analysing appointments in isolation (Chapter 4). By simulation, the performance of the approximation model is determined and subsequently improved by altering the configuration (Chapter 5).

Results from the data analysis (Chapter 3) are input variables for both models with respect to the arrival distribution and appointment probabilities. The requested capacity for appointments during the NCT phase and Review phase is approximated by the simulation model which based on historical arrivals and protocols.

For the initial configuration, we model the standard appointments as well as the appointments related to the sentinel node procedure and the first chemotherapy treatment as queuing nodes. The approach is similar to the approach used by Thomas et al. (2001). The determined service rate is rounded to the nearest higher integer making it implementable in weekly time slot schedules. This serves as input for the simulation model. The simulation model comprises the entire CP to address both goals. The model simulates the arrival of patients, the planning of appointments, the execution of the appointments and discharge of patients once all required appointments are performed. Different experiments are performed with varying time slot configurations and arrival rates as Brenner et al. (2009) researched for the ED (Chapter 6). Figure 13 shows the overview of our approach.

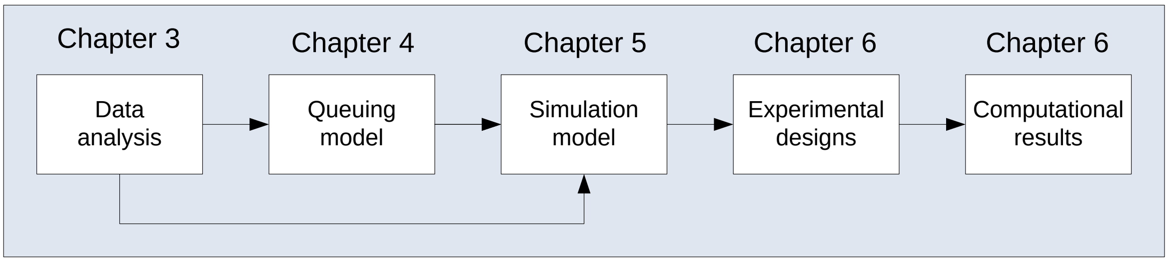

Figure 13: Approach

4 Queuing model

In this section we describe the queuing model that leads to the initial configuration. This is an approximation of the required capacity of each appointment type to establish a throughput time until chemotherapy of maximum two weeks for at least 90% of the regular patients. Furthermore, the results of the queuing model serve as input for the simulation model. Section 4.1 discusses the assumptions of the approach. The performance measures are stated in Section 4.2. Section 4.3 presents the results the queuing model.

4.1 Assumptions

We consider each appointment type in isolation on a weekly basis. Thus, each appointment is modelled as one queue. At arrival, patients are homogeneous since they are indistinguishable from a medical point of view. Hence, one class of patients is used. To characterise the queuing model, we use Kendall's notation with the arrival process, service process and number of servers (Winston, 2004).

4.1.1 Arrival process

Many studies incorporate Poisson distributions to model the arrival of patients (e.g. Thomas et al., 2001; Singh, (2006); Maridah and Basri, 2013). Performing a goodness-of-fit test using a one sample Kolmogorov-Smirnov (K-S) test (p-value = 0.981), no statically significant difference is observed in the weekly arrivals in the period 2012-2013 and the Poisson distribution with corresponding mean λ. Thus, the arrival of patients at the neoadjuvant chemotherapy CP can be modelled using a Poisson process. See Appendix D for the SPSS output.

4.1.2 Service process

Although service times are unknown, probability distributions must be selected. We include exponentially distributed service times with mean $\mathbb{E}(S)$ and service rate $\mu = 1/\mathbb{E}(S)$. We use the exponential distribution as it includes higher variation than the actual distribution presumably has. Hence it results in a conservative approximation (i.e. more required capacity) as it forms an upper bound for the service time.

4.1.3 Servers

For every appointment type, one server is included as we treat every appointment type as a single entity.

Combining the characteristics of the arrival process, service process and the number of servers we use an M/M/1 model.

4.2 Performance measures

Following from the main objective, we want to approximate the weekly service rate per appointment, required to serve 90% of the patients within two weeks. Since appointments are scheduled in a semi-fixed sequence, the period in which each appointment is allowed to be scheduled is less than two weeks. But, as appointment sets vary over patients, it is impossible to determine these periods. Therefore, the approximation model includes equal service level for all appointment types. The service rate is determined in order to serve at least 90% of the patients within two time periods.

An often used performance measure in queuing theory is the load, or the fraction of time a server is working (denoted by ρ; $\rho = \lambda/\mu$). For a stable system it is required that the mean service rate (denoted by μ) should be greater than the mean arrival rate (denoted by λ). Otherwise, the queue length grows to infinity. We calculate the r-th percentile of time in queue with the formula presented by Fenwick (2002), with the time period $\pi q(r)$ set to two and r = 90: $\pi q(r) = W * LN[100\rho/(100-r)]$, where $W = L/\lambda = 1/(\mu-\lambda)$ and $L = \rho/(1-\rho)$. Where W is the mean waiting time in the system and L is the mean number of patients in the system.

4.3 Results

This section discusses the computational results of the queuing model for all appointment types included in the ATP phase and the first chemotherapy treatment. The results are shown in Table 4. We conclude that the service rate should exceed the arrival rate by one patient per week (where μ is rounded up to the nearest integer). The integer values for the service rate for each appointment type serve as input parameters for the number of time slots in the simulation model. Appendix E shows the results for scenario 1-5.

Table 4: Queuing results (scenario data is obtained from 23-01-2012 until 06-12-2013 with N = 338 patients)

Appointment type	Input parameter	Output parameter	Output parameter
Node i	Arrival rate λ_i (per week)	Service rate μ_i (per week)	Service rate μ_i (per week; integer)
1. 1st appointment NP	3.30	4.31	5
2. Biopsy	2.37	3.35	4
3. MRI scan	2.83	3.83	4
4. ECG	2.95	3.96	4
5. PET/CT scan	2.85	3.85	4
6. EF	3.18	4.20	5
7. Ultrasonography breast	2.82	3.82	4
8. CRX	2.78	3.77	4
9. 2nd appointment NP	2.85	3.85	4
10. SNP	0.59	1.34	2
11. Internist	2.90	3.90	4
12. Consult outpatient clinic	2.89	3.89	4
13. 1st Chemotherapy treatment	3.05	4.06	5

5 Simulation study

In this chapter, the simulation study is discussed. We apply offline operational appointment planning to measure the performance of the system. We use a discrete-event simulation model. With simulation, the approximation model is validated and the performance of variations in configuration and other input parameters is assessed. We consider the steps in a simulation study presented by Law (2007) as an appropriate roadmap. The steps are shown in Figure 14.

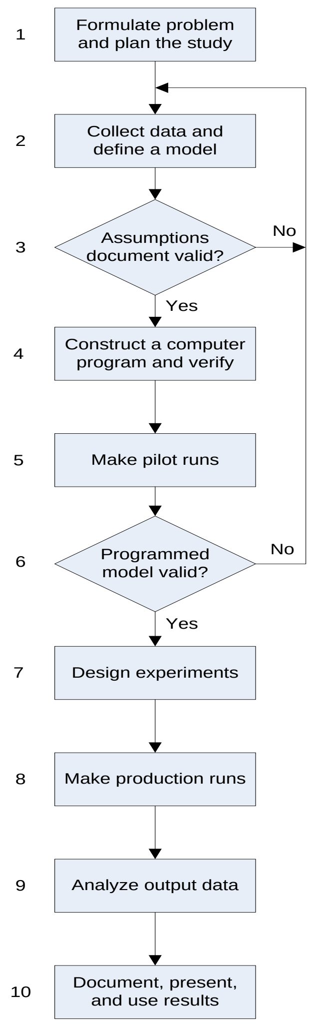

Figure 14: Steps in a simulation study. Law (2007)

Section 5.1 discusses the assumptions included in the simulation study. The performance measures are described in Section 5.2. Section 5.2 gives a description of the simulation model. The accuracy of the model is discussed in section 5.4. The experimental designs and computational results are presented in Chapter 6.

5.1 Assumptions

With the creation of a simulation model, restrictions are included that are not incorporated in the queuing model. Although many restrictions can be included, assumptions must be made since it is a simplified reproduction of the actual system. We list the assumptions:

- Patients are able to visit the hospital at any given time; the planned appointment date and time are the actual appointment date and time.

- No-shows are excluded and patient arrive exactly on time.

- The arrival rate is constant over the length of the simulation.

- As with the queuing model, we assume one available server for each appointment type (in the ATP phase and the first chemotherapy treatment). For some appointments this is reality (e.g. MRI scan and PET/CT scan) but for other appointments this is obviously a simplification of reality (e.g. NP's and internists). For the other appointments in the NCT phase and the Review phase, multiple servers are included as it significantly reduces the complexity of the model and still results in satisfying outcome.

- The presence of the standard appointments of the ATP phase for an individual patient are known at arrival. Same is true for the first chemotherapy treatment. Probabilities for different appointments are independent on each other.

- Absence of physicians nor downtimes of resource equipment are taken into account.

- Prior to the SNP, two appointments are necessary (POS and SNI). For simplicity, we consider these three appointments as one set (i.e. we include a single probability for SNP, the associated appointments are scheduled when the SNP is required).

- Seasonal effects are omitted. Arrivals are based on yearly averages.

- Data analysis shows that not all patients start with a chemotherapy type in accordance with the protocol. However, since this is a small group (2013: < 5%) and properties vary between patients in this group we exclude these chemotherapy types. They are substituted with proportionally AC and PTC.

- Recurring chemotherapy treatments are scheduled on the same day as the first chemotherapy treatment. All NP appointments, internist appointments and MRI scans during the NCT phase and the review phase are scheduled with certainty when treatments take place.

- The Outpatient Clinic currently plans appointments up to six week ahead. We include no such timeframe. For the first chemotherapy treatment it is required that the chemotherapy type is known two days in advance.

5.2 Performance measures

The relevant performance measures are different for the two goals of this study. For the primary goal, the service level, average throughput time and time slot utilisation are relevant performance measures. For the secondary goal, the requested number of appointments is determined. The measurements are listed below.

- Service level (percentage of patients start with the chemotherapy treatment within two weeks after arrival to the CP)

- Average throughput time (number of days between arrival to the CP and the first chemotherapy treatment)

- Utilisation time slots (ratio of available time slots filled)

- Average number of requested appointments per week

- Distribution of the number of requested appointment per week

5.3 Description of the simulation model

This section gives the description of the simulation model. The arrivals of patients, planning of the appointments, the processing of the appointments and discharge of patients are discussed in the following paragraphs.

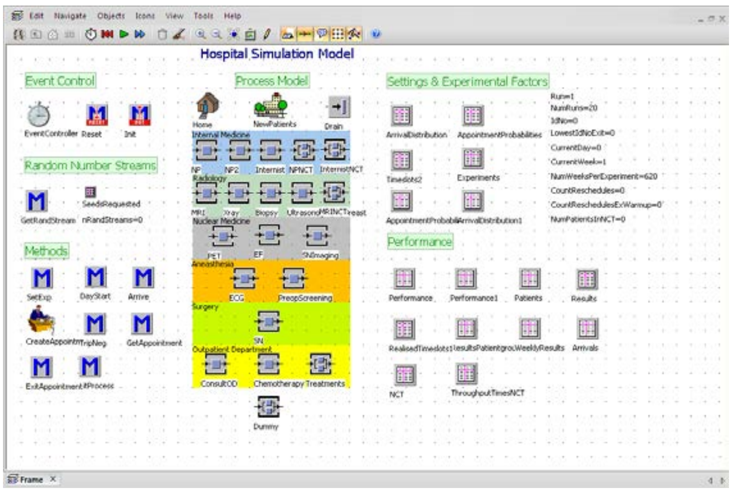

Figure 15: Screenshot of the Simulation Model

Figure 15 gives a screenshot of the model created in Technomatix Plant Simulation 10.1 (Siemens). The flow chart is which describes the process for an individual patient is shown in Figure 16.

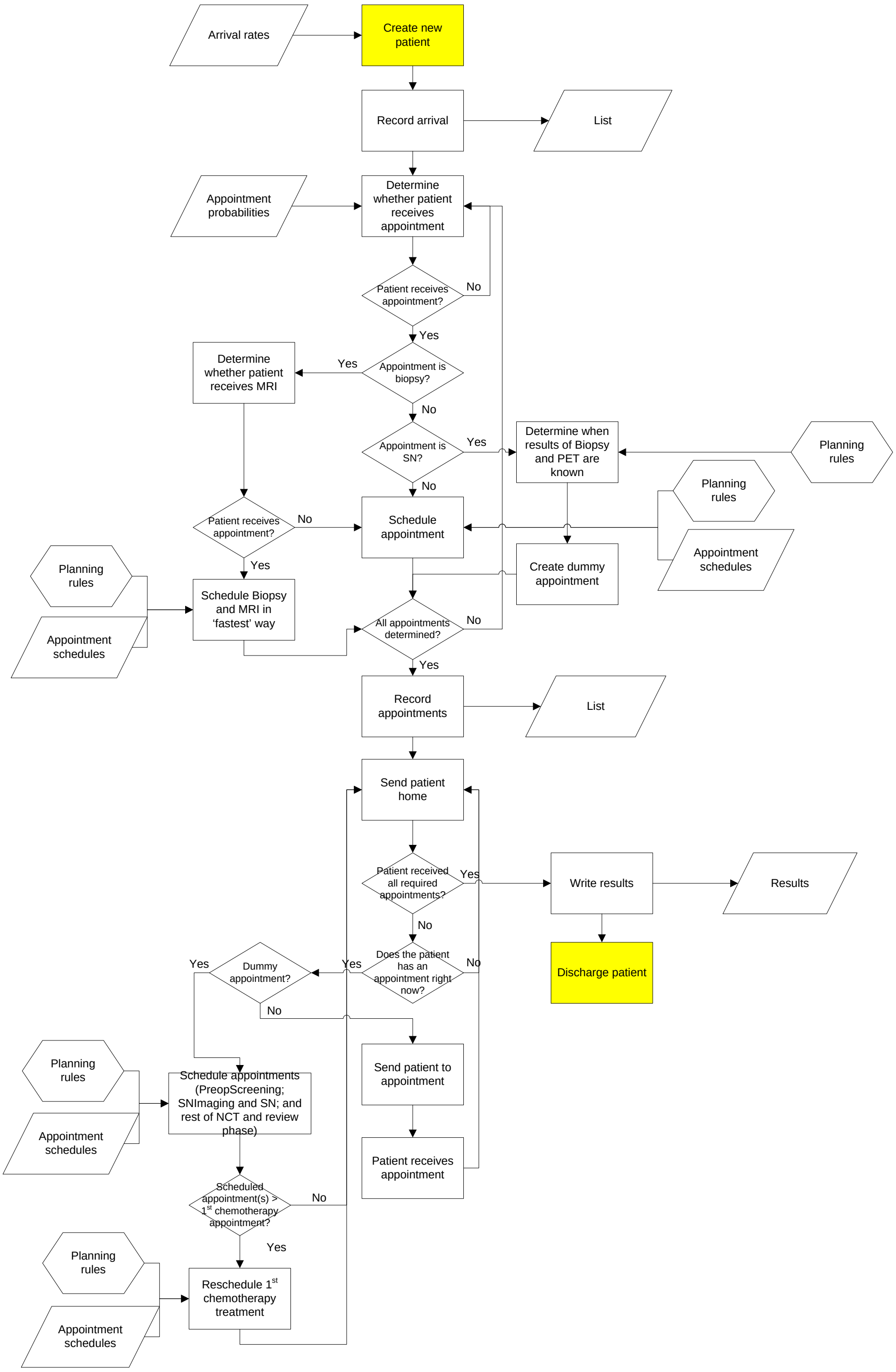

Figure 16: Flowchart of the simulation process (for an individual patient)

5.3.1 Patient arrival

Every workday, patients arrive at 13:15. This corresponds to the time patients start with the CP once the results of the outpatient breast clinic are communicated with the patient. For the arrival distribution, we differentiate between weekdays. Table 5 shows that Mondays and Thursday form the vast majority of the arrivals as the outpatient breast clinic is scheduled on these days.

The Poisson distribution is included to model patient arrivals. Performing a goodness-of-fit test using a one sample Kolmogorov-Smirnov (K-S) test (minimum p-value = 0.998), no statically significant difference is observed in the daily arrivals in the period 2012-2013 and the Poisson distribution with corresponding mean λ (see Appendix D for the SPSS output). Thus, the arrival of patients at the neoadjuvant chemotherapy CP can be modelled using a Poisson process. The difference in performance between the inclusion of historical arrivals and Poisson arrivals is discussed in the following section.

Table 5: Arrival rates

	Mean arrival rate	Mean arrival rate (+5%)	Mean arrival rate (+10%)	Mean arrival rate (+20%)	Mean arrival rate (+50%)	Mean arrival rate (-20%)
Monday	1.37	1.44	1.51	1.64	2.06	1.10
Tuesday	0.16	0.17	0.18	0.19	0.24	0.13
Wednesday	0.19	0.20	0.21	0.23	0.29	0.15
Thursday	1.60	1.68	1.76	1.92	2.40	1.28
Friday	0.13	0.14	0.14	0.16	0.20	0.10
Total	**3.19**	**3.63**	**3.80**	**4.14**	**5.19**	**2.76**

5.3.2 Appointment planning

At arrival, the presence of each appointment type in the ATP phase and for the first chemotherapy treatment is determined. Instantly, taking the appointment restrictions into account, appointment dates and times are established. A patient is assigned to the first feasible time slot. Since the MRI scan should be planned prior to biopsy or five days after biopsy, both schedules are determined after which the schedule with the earliest completion date (i.e. date when all results are known) is selected. The SNP is planned once the results of the PET/CT scan and the biopsy are known. If the SNP is not feasible to be planned prior to the first chemotherapy treatment, the first chemotherapy treatment is rescheduled. The remaining appointments in NCT phase and Review phase are simultaneously planned for SNP patients. For regular patients, these appointments are planned at arrival.

Once all appointments are scheduled, the patient is sent home. The included appointment restrictions and appointment probabilities are listed in respectively Appendix F and Appendix G.

5.3.3 Appointments

When an appointment commences, the patient is sent to the server at the corresponding date and time. The patient receives immediate service for a period of time (see Appendix H for appointment durations).

Upon completion, the received service is recorded and the patient is sent home again. For all appointments, one server treats the patients. In other words, at most one patient is allowed to be served by the same human or equipment resource at any given time.

The time slot configuration modelled in the simulation model is for each appointment type relating to the first objective, the number of time slots per week. We refer to the time slot allocation as schedule with the days on which time slots are scheduled and their corresponding starting times. The default allocation is a schedule with possible time slots based on the appointment restrictions, appointment durations, appointment probabilities and arrival distributions. The allocation is for every week the same, thus we include weekly rosters. See Appendix I for the allocation of the time slots.

5.3.4 Discharge

A patient exits the CP when all required appointments are received. Just before discharge, the desired data is stored.

5.4 Accuracy of the simulation model

To show the accuracy of the simulation model, the verification, the validation and the use of common random numbers are discussed in this section. Besides, the warm-up period, the number of replications and the number of runs included in the study are determined in order to achieve reliable results. These numbers are determined with the current arrival rate and the queuing results as input configuration. For the primary problem, simulation of an individual patient terminates after the first chemotherapy treatment is dosed as it significantly reduces the simulation time. For the secondary problem, simulation of an individual patient terminates after the last appointment in this CP. This results in varying warm-up periods, run lengths and number of runs required for both problems as is discussed in the following paragraphs. Therefore, for the calculation of the warm-up period, run length and number of runs we pretend that both parts of the process are simulated with different models.

5.4.1 Verification

According to Law (2007), verification is concerned with debugging of the simulation computer program. Since the final model runs without errors, the model is debugged. Another technique for verification is the use of animation. Animation is used to represent the patients on the screen that dynamically change position in the CP. Concurrent animation is used; animation that is being displayed at the same time that the simulation is running. By doing so, unforeseen behaviour of the model can be detected (e.g. patients stuck at home or at an appointment). By simulating extreme cases (e.g. low appointment probabilities or high utilisation), we check whether the output is still feasible and consistent with our expectations.

5.4.2 Validation

Maull, Smart, Harris and Karasneh (2009) describe the validation of simulation studies depending on the availability of real data. Three possible situations are 1) no real data, 2) real output data and 3) real input and output data. Since our simulation model reflects a nonexistent situation at the hospital, no real output data is available. Nevertheless, we can validate the simulation model by discussing it with staff and comparing the simulated input parameters with the available data. We discussed the included restrictions with the planner of the appointments and the restrictions, as well as the flow chart of the process with the manager. Minor modifications were implemented.

Law (2007) defines validation as the process of determining whether a simulation model is an accurate representation of the system, for the particular objectives of the study. Since the objective is to achieve a service level of at least 90% of the regular patients being treated within two weeks, we simulate the process with both historical distributions and Poisson distributions to determine whether there is a significant difference in performance. As problems arise when a high number of patients arrive in a short period of time, the distribution of the arrivals is important for the performance of this process.

Table 6 shows similar performance for both settings. The 95% confidence intervals show no significant difference between both distributions. Therefore, we use the Poisson distribution to model the patient arrivals. Furthermore, since the simulated input parameters are significantly similar to the data, we conclude that the simulation model is validated.

Table 6: Performance of the simulation model (20 runs of 620 weeks with a warm-up period of 100 weeks)

Input	Arrivals	Average throughput time	Service level
Arrivals (historical data)	[1781, 1830]	[11.97, 12.46]	[84%, 89%]
Arrivals (Poisson distribution)	[1762, 1814]	[11.87, 12.49]	[85%, 90%]

5.4.3 Common random numbers

In order to compare configurations, common random numbers are used. Thus, the same probabilities are used to determine probability distributions. This makes experiments comparable. Consequently, the same patient arrival patterns and appointment probabilities are used. Along with equal initialisation rules create common random numbers differences in performance solely attributable to the different configurations and not to the occurrence of arrivals or appointments.

When arrival rates differ, different random number streams are used for different rates. Hereby, the differences in performance are not anymore solely attributable to different settings but also to differences in random numbers.

5.4.4 Warm-up period

The initial state of the simulation model is empty, which means that there are no patients in the CP nor any appointments planned. Since we are interested in the performance when the CP is operating "normally", we need to eliminate a period of results when the system is not yet in a steady state. By the graphical procedure of Welch presented by Law (2007), we set the length of the warm-up period to 100 weeks for both models. See Appendix J for the analysis of the warm-up period.

5.4.5 Run length

In order to obtain accurate estimations on performance, the model is required to simulate a minimum number of replications. Since weekdays are heterogeneous and weeks are homogeneous, we select a period of one week as the length of a replication. Weekdays differ since arrival rates vary significant and time slots are not equally distributed across days. We use the procedure presented by Law (2007) for establishment of the run length required to estimate the mean $\mu = E(X)$ within a 95%-confidence interval. This resulted in a minimum run length of 86 replications when only the first chemotherapy treatment is included. For the simulation model of the entire CP, the minimum run length is 129 replications.

As the warm-up period is deleted in performance measurement, we need to simulate the process for the first model for at least 186 weeks and for the first second model 229 weeks. We select 620 weeks as the run length for both models. With this setting, ten years of the process is analysed.

5.4.6 Number of runs

As each run is based on a set of random number streams, several runs are simulated with varying sets. We simulate 40 runs with the input of the queuing model and different random number streams and analyse the performance. For the performance of the first model we analyse the minimum number of runs for a statistically reliable number of arrivals, average throughput time (regular patients), average throughput time (regular and SN), service level (regular patients) and the service level (regular and SN). For all outcomes, 12 runs are sufficient. As this simulation model runs rather fast, we run each experiment for 20 runs.

For the performance of the NCT phase and Review phase, we determine the following performance measures: the average number of consults at the Outpatient Clinic, the average number of treatments, the average number of NP appointments, the average number of MRI appointments and the average number of internist appointments. For all outcomes, 6 runs are sufficient. We select 10 runs as the number of runs use in the experiments.

5.5 Conclusion

A validated and verified simulation model is constructed. The model is appropriate to analyse both the APT phase and the entire CP. Different arrival scenarios are defined for which experiments are established in the next chapter.

6 Computational results

This chapter presents the results of the simulation study. Section 6.1 describes the experimental design which explains the procedures to determine the required outcomes. The results of the experiments are shown in Section 6.2. In Section 6.3, the results are discussed.

6.1 Experimental design

As we have two goals in this study, two experimental designs are included. Paragraph 6.1.1 discusses the experimental design to find the required capacity in order to start the chemotherapy treatment for at least 90% of the regular patients within 14 days after arrival. Besides, experiments are established to determine the consequences when all patients require biopsy. Furthermore, the effect of high utilisations regarding the service level is determined. Paragraph 6.1.2 describes the experimental design to determine the requested number of appointments during the NCT phase and Review phase. For both designs, the scenarios defined in Section 5.3 are simulated.

6.1.1 Service level

Attaining the desired service level is the main objective in this experimental design. We differentiate between three situation in each scenario. First, the required time slots are determined to achieve the desired service level for default settings. Default settings are the current appointment probabilities and default time slot allocation. Second, the same procedure is performed when all patients require biopsy. Third, we analyse the impact of high utilisation for certain appointment types. A number of additional experiments are executed to assess the impact of time slot alignment and the consequences of utilisation on waiting times.

Default settings

In order to achieve the desired service level, the input from the queuing model is optimised by modifying the number of time slots. Although the inclusion of a 2^k factorial design is a more economical strategy than the one-factor-at-a-time (OFAT) approach, we select the latter approach (Law, 2011). In the same context Andradóttir (1998) discusses the issue of finding the appropriate configuration with simulation when the total number of possible configurations is high. He starts with a broad dispersion where configurations that appear to result in good solutions are derived. The remaining configurations are then further examined. As 15 appointments are included, the 2^k factorial design would result in more than 30,000 factor combinations (i.e. simulation runs) when only two situations per appointment are considered. Promising modifications are combined, starting with two modifications per experiment. Configurations are regarded as promising when significant increase in service level is measured compared to the queuing configuration or little decrease (when the number of time slots is reduced).

Through the simulation of a number of pilot runs, we differentiate between crucial appointments in the CP and less crucial appointments. Crucial appointments are the first NP, the MRI scan, the biopsy, the chemotherapy treatment, the internist appointment and the consult at the Outpatient Clinic. These appointments are regarded as crucial since appointment planning restrictions and pilot runs show that modifications in time slots have significant influence on performance. All others are considered as less influential on the performance. Although the data analysis shows that the PET/CT scan and EF are bottlenecks in the current situation, their impact on the throughput time in the simulation model is limited. This is because appointment planning restrictions show allowable delay for both appointment types without increasing the throughput time.

The distinction serves to focus the modifications in the number of time slots on these crucial appointments. With this approach, the complexity of the problem significantly reduces.

The following procedure is used to find the optimal configuration for the scenarios:

1. Determine performance queuing model (with modifications as the previous scenario resulted in a minimum number of time slots for appointment *i* that is higher than the queuing model suggests).

2. Analyse the waiting time and utilisation of less crucial appointments and modify when feasible.

3. Combine modifications in the number of time slots for crucial appointments.

4. Determine performance of promising combinations.

When the service level is attained, determine whether the number of time slots of less crucial appointments (starting with the appointment type with the lowest utilisation) can be decreased while attaining the service level.

All patients require biopsy

The probability of the biopsy appointment for an arbitrary patient is currently under 75%. New developments in the process show that every patient receives this appointment to be independent on the reports from other hospitals. Therefore, we simulate the consequences when every patient has a biopsy for all scenarios. The configurations are based on the results of the current setting (i.e. with probabilities for biopsy based on the data). Modifications are made when the service level is no more attained.

High utilisation

Besides the optimal time slot configuration for each scenario in both settings, we determine the impact on the service level of high utilisations. Particularly, the utilisation of the time slots for the MRI scan, PET/CT scan, EF and internist are desired to be as high as possible since the current utilisation of each of these appointment types is high. Since waiting times are currently high, as is shown in Chapter 2, low utilisation of these time slots are possible not accepted by the involved departments. Therefore, we simulate the CP with the highest possible utilisation of the time slots of these appointments. For simplicity we refer to these appointments as scarce appointments.

Additional experiments (Base Scenario)

As discussed in Paragraph 5.3.3, the day and time of available time slots is equal in all experiments. To indicate the necessity of time slot alignment, we simulate different allocations. We establish besides the default allocation four additional allocations (see Table 7).

Table 7: Allocations

Allocation	Description
Default	time slots are assigned with consideration of appointment planning restrictions
Every Day	time slots of all appointment types are evenly distributed over weekday in a chronological manner
Default + 1 Day	time slots in the default allocation are shifted one day ahead
Random	time slots are assigned without consideration of appointment planning restrictions
Wrong	time slots are deliberately allocated to 'wrong' days and times with regard to appointment planning restrictions

Furthermore, we analyse the performance of different utilisations by observing the waiting times. Besides, the use of biweekly allocation is researched. This includes a different number of time slots for even and odd week numbers. By introducing biweekly rosters, capacity can be more accurately aligned with demand. All additional experiments are performed for the Base Scenario.

6.1.2 Number of appointments

As for the appointments subsequent to the first chemotherapy treatment no time slots are used, we approximate the number of patients required to be served per week. We distinguish between chemotherapy treatments, NP appointments, MRI scans and internist appointments. For all four we simulated the number of appointments requested per week.

6.2 Experimental results

This section presents the results of the experiments for all scenarios.

6.2.1 Base scenario

This scenario results in the expected number of time slots required in the current situation. The configuration established by the queuing model results in an inadequate service level of 85-90% (see Appendix K). The addition of one time slot does not result in sufficient improvement. The addition of one non crucial appointment results in no significant effect on the service level. Distributing two time slots over the six crucial appointments results in 15 experiments. As two additional time slots still not result in the required service level, we run experiments with three additional time slots for the crucial appointments. With six appointments and three time slots, we construct 20 experiments assuming that each appointment includes one or no extra time slots. The results are shown in Appendix K. Of the 20 experiments, eight result in a sufficient service level.

The result of the preferred configuration is shown in Table 8. Experiment B.2 shows the results with four additional time slots for the crucial appointments, but one time slot less for the EF. Experiments BS.1 and BS.2 use rather different configurations but result in similar performance. We prefer experiment BS.1, as it requires less capacity from the four scarce appointment types. The utilisation of the time slots for biopsy is relatively low. The average utilisation of the time slots for the standard appointments is 65%. When all patients require biopsy, little additional capacity is required. It might seem incongruous that additional time slots are required for appointments besides biopsy but as these appointments occasionally result in delay in the CP, the service level increases when capacity is increased. For high utilisation of time slots for the four scarce appointments, the consequences are clear. Waiting times increase significantly as utilisation exceeds 90% (experiment BS.4). Experiment BS.5 shows that the service level is attained when the utilisation of these four appointments is under 80%.

The configuration with the lowest feasible number of time slots for each appointment type results in a service level of [41%, 49%] and an average utilisation of 74%. This configuration sets the number of time slots for each appointment type to four besides the biopsy appointment (three time slots) and the POS, SNI and SNP (one time slot). The number of time slots is considered feasible if the utilisation is under 90%. When the utilisation is over 90% and the arrival rate is smaller than the service rate, the solution is theoretically feasible but not in practice as high waiting times are created.

Table 8: Results for Base Scenario

Base Scenario (current arrivals)	Normal settings		100% Biopsy	High utilisation	
Experiment (#)	BS.1	BS.2	BS.3	BS.4	BS.5
NP1	6 [54%, 55%]	5 [65%, 67%]	6 [54%, 55%]	6 [54%, 55%]	6 [65%, 67%]
MRI	4 [70%, 72%]	5 [56%, 57%]	5 [56%, 57%]	3 [93%, 96%]	4 [70%, 72%]
PET	4 [69%, 71%]	4 [69%, 71%]	4 [69%, 71%]	3 [92%, 96%]	4 [69%, 71%]
EF	5 [62%, 64%]	4 [78%, 80%]	4 [78%, 80%]	4 [78%, 80%]	4 [78%, 80%]
Biopsy	5 [45%, 47%]	5 [45%, 47%]	6 [56%, 58%]	5 [45%, 47%]	5 [45%, 47%]
Chemotherapy	5 [62%, 64%]	5 [62%, 64%]	5 [62%, 64%]	6 [52%, 53%]	6 [51%, 53%]
ECG	4 [70%, 72%]	4 [70%, 72%]	4 [70%, 72%]	5 [56%, 58%]	4 [70%, 72%]
Ultrasonography Breast	4 [67%, 70%]	4 [67%, 70%]	4 [67%, 70%]	5 [54%, 56%]	4 [67%, 70%]
CRX	4 [68%, 70%]	4 [68%, 70%]	4 [68%, 70%]	5 [54%, 56%]	4 [68%, 70%]
NP2	4 [69%, 72%]	4 [69%, 72%]	4 [69%, 72%]	5 [56%, 57%]	4 [69%, 72%]
Internist	4 [73%, 76%]	5 [59%, 60%]	5 [59%, 60%]	3 [98%, 99%]	4 [73%, 76%]
Consult OC	5 [58%, 60%]	5 [58%, 60%]	5 [58%, 60%]	5 [58%, 60%]	5 [58%, 60%]
SNP	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]
POS	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]
SNI	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]	2 [29%, 31%]
Service level	[90%, 94%]	[90%, 95%]	[90%, 95%]	[7%, 15%]	[90%, 94%]
Average utilisation	65%	65%	65%	67%	65%
Average throughput Time (in days)	[11.4, 11.9]	[11.3, 11.9]	[12.0, 12.5]	[45.3, 90.4]	[11.2, 11.9]

Additional experiments

Table 9 shows the performance of the established allocations for the Base Scenario. All experiments are simulated with the number of time slots in accordance with the preferred configuration (experiment BS.1 in Table 8). Therefore, merely the allocation of the time slots differs among experiments.

We conclude that all modifications show significant decrease in service level. The average throughput time is slightly higher for Every Day and Default + 1 Day. When time slots are wrongly allocated, performance is worse than in the current situation (see Section 3.3). Both the service level and average throughput time are better in the current situation even though significantly less capacity is required since no time slots are used. The number of hospital visits required until the first chemotherapy treatment is the lowest for the default allocation. Wrong alignment of time slots leads to additional hospital visits. Figure 17 shows the distribution of the throughput time until the first chemotherapy treatment. Graphs are angular shaped as time slots are allocated to specific days. When time slots are dispersed over the weekdays, the graph shows a more smooth line.

Table 9: Results for different configurations (for the Base Scenario with preferred number of timeslots)

Configuration	Service level (regular patients)	Average throughput time (regular patients)	Average number of visits
Default	[90%, 94%]	[11.4, 11.9]	[4.6, 4.7]
Every day	[80%, 86%]	[11.8, 12.5]	[5.7, 5.8]
Default + 1 day	[73%, 79%]	[12.0, 12.6]	[5.3, 5.4]
Random	[62%, 68%]	[14.4, 15.1]	[6.0, 6.1]
Wrong	[5%, 6%]	[22.5, 23.3]	[7.1, 7.2]

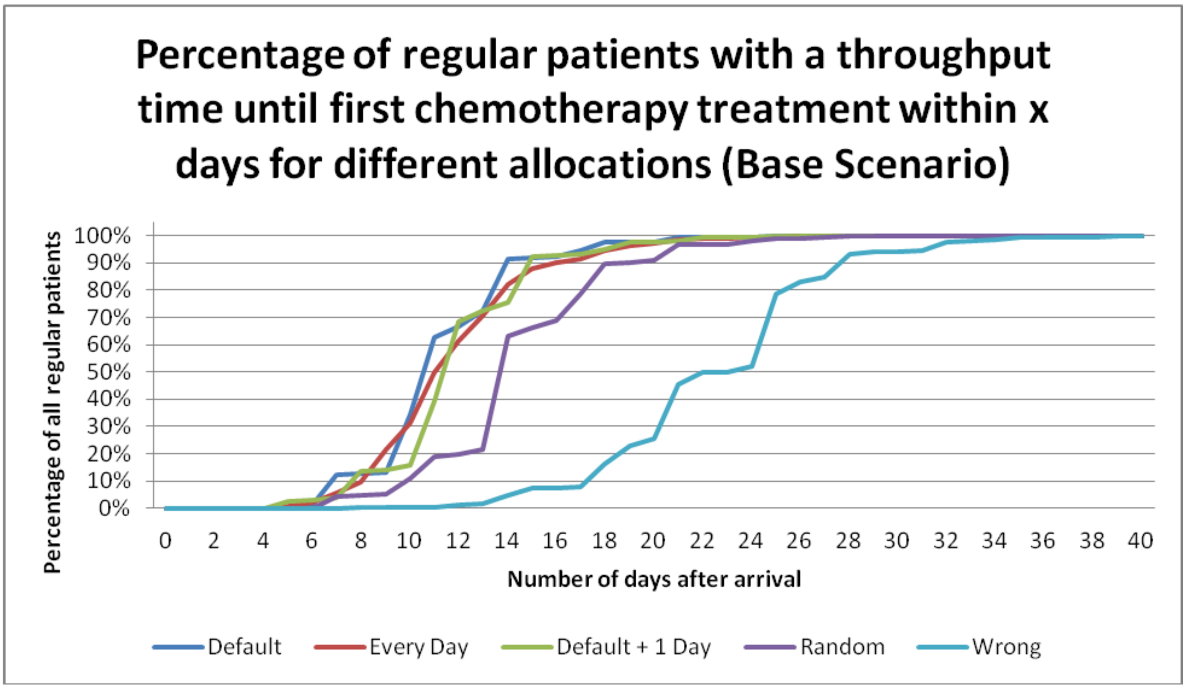

Figure 17: Throughput time distribution for regular patients with different allocations (Base Scenario)

The impact of utilisation of EF time slots on the waiting time for an EF appointment is shown in Figure 18. The blue line represents the waiting time distribution for the EF appointment in experiment BS.5. As expected, waiting times increase when utilisation increases. While 90% of the appointment is planned within eight days with an utilisation of 79%, the number of days increases to 13 days when the utilisation is 85%. This high increase in waiting time caused by a relatively small increase in utilisation is observed for other appointments as well. For all other non crucial appointments, graphs are similar as appointment restrictions are rather similar. We see that a utilisation of 88% or higher results for 90% of the appointments in a maximum waiting time over two weeks.

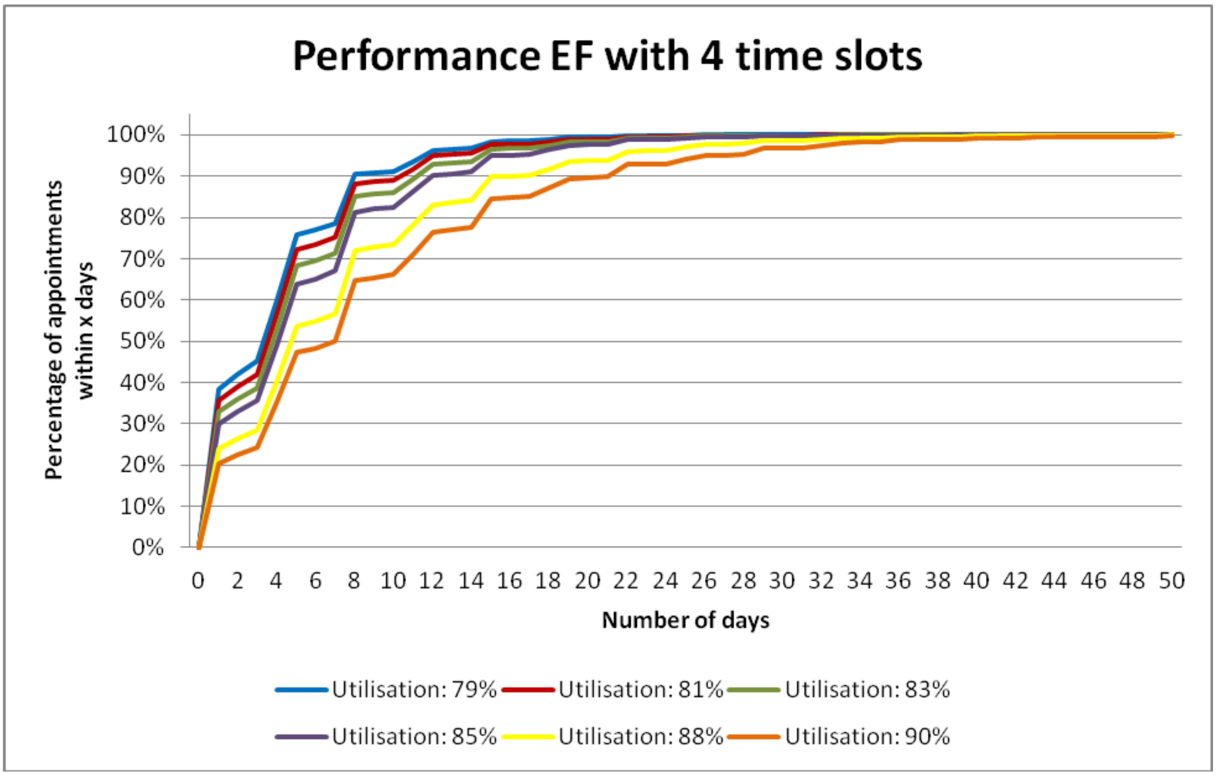

Figure 18: Performance 4 EF time slots

The impact of increasing utilisation of non crusial appointments through biweekly schedules is shown in Figure 19. EF is excluded as the utilisation is approximately 80% with weekly schedules. For all other non crucial appointments, utilisation is approximately 70% with weekly schedules and approximately 80% with biweekly schedules. In the biweekly schedules, one time slot is subtracted from the odd week numbers. It is evident that the appointment types with significantly similar utilisations perform likewise. On average, with a utilisation of approximately 70%, nearly all appointments (> 99%) can be planned within 14 days. With a utilisation of approximately 80%, a significant part of the appointments (> 5%) cannot be planned within 14 days. The performance of several configurations with the inclusion of biweekly schedules is shown in Appendix K. When the utilisation of the non crucial appointments ECG, ultrasonography, CRX and NP2 are desired to be approximately 80%, we see that the desired service level is not attained. When biweekly schedules are also applied for other appointments, we see that the average utilisation is increased to 74%. However, the service level is significantly lower than with weekly schedules. See Appendix I for the results.

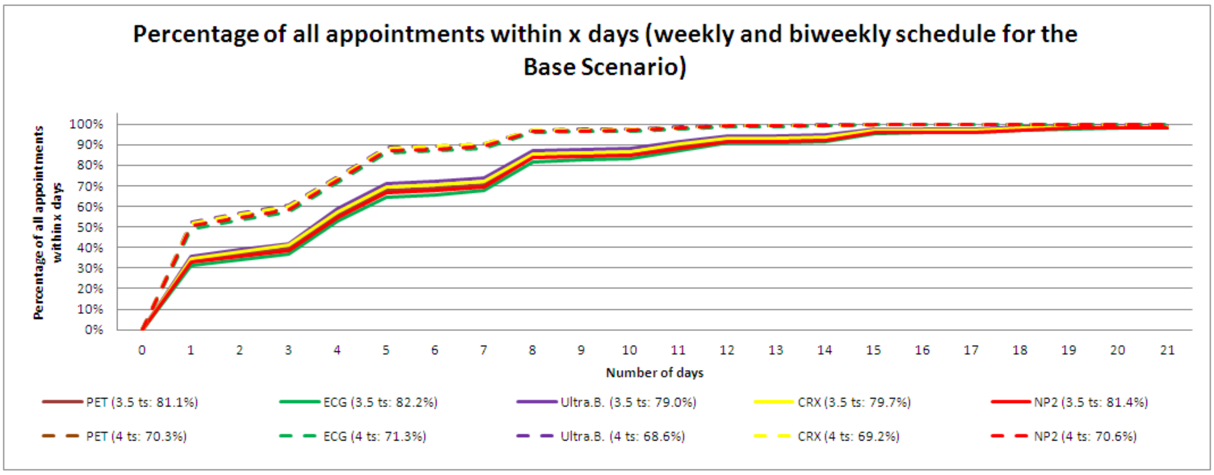

Figure 19: Waiting time for non crucial appointments except EF (weekly and biweekly schedule; 3.5 ts stands for 3 time slots for odds weeks and 4 time slots for even weeks; percentage between brackets is utilisation of time slots)

6.2.2 Scenario 1

The queuing model suggests that for an increase of 5% in the arrival rate, three additional time slots are required, compared to the current situation. For the ECG, the internist appointment and the consult at the outpatient department, one time slot should be added. As three additional time slots (compared to the queuing results for the base scenario) are insufficient to attain the service level, four additional time slots are simulated resulting in 15 experiments. Table 10 shows that the optimal configurations require additional time slots for the internist and the consult at the outpatient clinic, but not for the ECG. Increasing the number of time slots with two at a single appointment type results in insignificant improvement in performance.

Experiments S1.1-S1.3 include the same total number of time slots but vary in numbers for the first appointment with the NP, the MRI scan and the first chemotherapy treatment. The capacity of the MRI scan is considered the most valuable of these three appointments and we prefer one time slot more for the first NP over one for the first chemotherapy treatment. Consequently, the configuration in experiment S1.1 is the preferred choice. Compared to experiment S1.3, one additional MRI scan and one biopsy time slot are required to be able to dose at least 90% of all regular patients within two weeks when all patients require biopsy. When the utilisation of the scarce appointments is desired to be as high as possible, the service level only slightly decreases (experiment S1.6).

Table 10: Results for Scenario 1

Scenario 1 (+ 5% arrivals)	Normal settings			100% Biopsy		High utilisation
Experiment (#)	S1.1	S1.2	S1.3	S1.4	S1.5	S1.6
NP1	6 [57%, 58%]	5 [68%, 70%]	5 [68%, 70%]	5 [68%, 70%]	6 [57%, 58%]	6 [57%, 58%]
MRI	4 [73%, 75%]	5 [59%, 60%]	4 [73%, 75%]	5 [59%, 60%]	5 [59%, 60%]	4 [73%, 75%]
PET	4 [73%, 75%]	4 [73%, 75%]	4 [73%, 75%]	4 [73%, 75%]	4 [73%, 75%]	4 [73%, 75%]
EF	5 [66%, 67%]	5 [66%, 67%]	5 [66%, 67%]	5 [66%, 67%]	5 [66%, 67%]	4 [82%, 84%]
Biopsy	5 [48%, 49%]	5 [48%, 49%]	5 [48%, 49%]	6 [59%, 61%]	6 [59%, 61%]	5 [48%, 49%]
Chemotherapy	5 [65%, 67%]	5 [65%, 67%]	6 [54%, 56%]	6 [54%, 56%]	5 [65%, 67%]	6 [54%, 56%]
ECG	4 [74%, 76%]	4 [74%, 76%]	4 [74%, 76%]	4 [74%, 76%]	4 [74%, 76%]	4 [74%, 76%]
Ultrasonography Breast	4 [71%, 73%]	4 [71%, 73%]	4 [71%, 73%]	4 [71%, 73%]	4 [71%, 73%]	4 [71%, 73%]
CRX	4 [72%, 74%]	4 [72%, 74%]	4 [72%, 74%]	4 [72%, 74%]	4 [72%, 74%]	4 [72%, 74%]
NP2	4 [73%, 75%]	4 [73%, 75%]	4 [73%, 75%]	4 [73%, 75%]	4 [73%, 75%]	4 [73%, 75%]
Internist	5 [62%, 63%]	5 [62%, 63%]	5 [62%, 63%]	5 [62%, 63%]	5 [62%, 63%]	4 [77%, 79%]
Consult OC	5 [61%, 63%]	5 [61%, 63%]	5 [61%, 63%]	5 [61%, 63%]	5 [61%, 63%]	5 [61%, 63%]
SNP	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]
POS	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]
SNI	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]	2 [31%, 33%]
Service level	[90%, 94%]	[90%, 93%]	[90%, 93%]	[90%, 94%]	[90%, 94%]	[85%, 91%]
Average utilisation	67%	67%	67%	67%	67%	69%
Average throughput time (in days)	[11.5, 11.8]	[11.5, 11.9]	[11.3, 11.7]	[12.1, 12.5]	[12.1, 12.4]	[11.7, 12.6]

6.2.3 Scenario 2

For Scenario 2, one configuration performs best (see Table 11). When all patients require biopsy, one additional time slot for biopsy and the ECG, CRX or NP2 are required. We prefer lower utilisation of the time slots for ECG over CRX and NP2 (experiment S2.3). For the lowest feasible number of time slots for the four scarce appointments, the service level significantly decreases (experiment S2.4).

Table 11: Results for Scenario 2

Scenario 2 (+ 10% arrivals)	Normal settings		100% Biopsy		High utilisation	
Experiment (#)	S2.1		S2.3		S2.4	
NP1	6	[60%, 61%]	6	[60%, 61%]	6	[60%, 61%]
MRI	5	[62%, 63%]	5	[62%, 63%]	4	[77%, 79%]
PET	4	[77%, 79%]	4	[77%, 79%]	4	[77%, 79%]
EF	5	[69%, 71%]	5	[69%, 71%]	4	[86%, 89%]
Biopsy	5	[50%, 52%]	6	[63%, 64%]	5	[50%, 52%]
Chemotherapy	6	[57%, 58%]	6	[57%, 58%]	6	[57%, 58%]
ECG	4	[78%, 80%]	5	[62%, 64%]	5	[62%, 64%]
Ultrasonography Breast	4	[75%, 77%]	4	[75%, 77%]	5	[60%, 62%]
CRX	4	[75%, 78%]	4	[75%, 78%]	5	[60%, 62%]
NP2	4	[77%, 79%]	4	[77%, 79%]	5	[62%, 63%]
Internist	5	[65%, 67%]	5	[65%, 67%]	4	[81%, 83%]
Consult OC	5	[64%, 66%]	5	[64%, 66%]	5	[64%, 66%]
SNP	2	[32%, 35%]	2	[32%, 35%]	2	[32%, 35%]
POS	2	[32%, 35%]	2	[32%, 35%]	2	[32%, 35%]
SNI	2	[32%, 35%]	2	[32%, 35%]	2	[32%, 35%]
Service level	[90%, 94%]		[90%, 94%]		[76%, 83%]	
Average utilisation	68%		68%		67%	
Average throughput time (in days)	[11.3, 11.8]		[12.1, 12.4]		[12.6, 13.7]	

6.2.4 Scenario 3

In Scenario 3, the required number of time slots are relatively similar for all standard appointments. The input from the queuing model should be modified with three additional time slots for crucial appointments (i.e. first NP, biopsy and chemotherapy treatment). When all patients require biopsy, one additional time slot for biopsy is sufficient (experiment S3.2). The service level slightly decreases, but remains satisfactory. For high utilisation of the four scarce appointments, we show three configurations in Table 12. The service level is significantly lower [38%, 56%] when these appointments are maximally utilised. When one time slot is added to the appointment type with the highest utilisation, the service level increases. Repeating this procedure once more results in a significant higher service level (experiment S3.5).

Table 12: Results for Scenario 3

Scenario 3 (+ 20% arrivals)	Normal settings		100% Biopsy		High utilisation					
Experiment (#)	S3.1		S3.2		S3.3		S3.4		S3.5	
NP1	6	[65%, 67%]	6	[65%, 67%]	6	[65%, 67%]	6	[65%, 67%]	6	[65%, 67%]
MRI	5	[67%, 68%]	5	[67%, 68%]	4	[84%, 86%]	4	[84%, 86%]	4	[84%, 86%]
PET	5	[67%, 68%]	5	[67%, 68%]	4	[83%, 86%]	4	[83%, 86%]	4	[83%, 86%]
EF	5	[75%, 77%]	5	[75%, 77%]	4	[94%, 96%]	5	[75%, 77%]	5	[75%, 77%]
Biopsy	5	[55%, 56%]	6	[68%, 70%]	5	[55%, 56%]	5	[55%, 56%]	5	[55%, 56%]
Chemotherapy	6	[62%, 64%]	6	[62%, 64%]	6	[62%, 64%]	6	[62%, 64%]	6	[62%, 64%]
ECG	5	[68%, 69%]	5	[68%, 69%]	5	[68%, 69%]	5	[68%, 69%]	5	[68%, 69%]
Ultrasonography Breast	5	[65%, 67%]	5	[65%, 67%]	5	[65%, 67%]	5	[65%, 67%]	5	[65%, 67%]
CRX	5	[66%, 68%]	5	[66%, 68%]	5	[66%, 68%]	5	[66%, 68%]	5	[66%, 68%]
NP2	5	[67%, 69%]	5	[67%, 69%]	5	[67%, 69%]	5	[67%, 69%]	5	[67%, 69%]
Internist	5	[71%, 72%]	5	[71%, 72%]	4	[88%, 91%]	4	[88%, 91%]	5	[71%, 73%]
Consult OC	5	[70%, 72%]	5	[70%, 72%]	5	[70%, 72%]	5	[70%, 72%]	5	[70%, 72%]
SNP	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]
POS	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]
SNI	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]	2	[35%, 38%]
Service level	[92%, 95%]		[90%, 93%]		[38%, 56%]		[61%, 72%]		[80%, 87%]	
Average utilisation	67%		68%		73%		72%		70%	
Average throughput time (in days)	[11.3, 11.6]		[12.3, 12.5]		[16.9, 27.1]		[14.3, 16.6]		[12.3, 13.3]	

6.2.5 Scenario 4

For Scenario 4, two configurations result in the best performance (see Table 13 and Table 14). We prefer one extra time slot for ultrasonography over the CRX. For the situation in which every patients requires a biopsy, five of additional time slots are required. When high utilisation of the time slots of the scarce appointments is desired, the impact on the service level is significant (Table 14).

Table 13: Results for Scenario 4 (a)

Scenario 4 (+ 50% arrivals)	Normal settings				100% Biopsy			
Experiment (#)	S4.1		S4.2		S4.3		S4.4	
NP1	7	[70%, 71%]	7	[70%, 71%]	8	[61%, 62%]	7	[70%, 71%]
MRI	6	[70%, 71%]	6	[70%, 71%]	6	[70%, 71%]	7	[60%, 61%]
PET	6	[70%, 71%]	6	[70%, 71%]	6	[70%, 71%]	6	[70%, 71%]
EF	6	[78%, 80%]	6	[78%, 80%]	6	[78%, 80%]	6	[78%, 80%]
Biopsy	6	[57%, 59%]	6	[57%, 59%]	8	[64%, 65%]	8	[64%, 65%]
Chemotherapy	7	[67%, 68%]	7	[67%, 68%]	8	[58%, 59%]	8	[58%, 59%]
ECG	6	[71%, 72%]	6	[71%, 72%]	6	[71%, 72%]	6	[71%, 72%]
Ultrasonography Breast	5	[82%, 83%]	6	[68%, 69%]	6	[68%, 69%]	6	[68%, 69%]
CRX	6	[69%, 70%]	5	[82%, 84%]	6	[69%, 70%]	6	[69%, 70%]
NP2	6	[70%, 71%]	6	[70%, 71%]	6	[70%, 71%]	6	[70%, 71%]
Internist	7	[63%, 65%]	7	[63%, 65%]	7	[63%, 65%]	7	[63%, 65%]
Consult OC	7	[63%, 64%]	7	[63%, 64%]	7	[63%, 64%]	7	[63%, 64%]
SNP	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]
POS	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]
SNI	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]
Service level	[91%, 93%]		[90%, 93%]		[91%, 93%]		[93%, 95%]	
Average utilisation	70%		70%		68%		68%	
Average throughput time (in days)	[11.3, 11.6]		[11.3, 11.7]		[12.1, 12.3]		[11.8, 12.0]	

Table 14: Results for Scenario 4 (b)

Scenario 4 (+ 50% arrivals)	High utilisation							
Experiment (#)	S4.5		S4.6		S4.7		S4.8	
NP1	6	[82%, 83%]	6	[82%, 83%]	6	[82%, 83%]	7	[70%, 71%]
MRI	5	[84%, 86%]	5	[84%, 86%]	5	[84%, 86%]	5	[84%, 86%]
PET	5	[84%, 85%]	5	[84%, 85%]	5	[84%, 85%]	5	[84%, 85%]
EF	5	[94%, 96%]	6	[78%, 80%]	6	[78%, 80%]	6	[78%, 80%]
Biopsy	5	[69%, 70%]	5	[69%, 70%]	5	[69%, 70%]	6	[57%, 59%]
Chemotherapy	6	[78%, 79%]	6	[78%, 79%]	6	[78%, 79%]	7	[67%, 68%]
ECG	5	[85%, 87%]	5	[85%, 87%]	5	[85%, 87%]	6	[71%, 72%]
Ultrasonography Breast	5	[82%, 83%]	5	[82%, 83%]	5	[82%, 83%]	6	[68%, 69%]
CRX	5	[82%, 84%]	5	[82%, 84%]	5	[82%, 84%]	6	[69%, 70%]
NP2	5	[84%, 86%]	5	[84%, 86%]	5	[84%, 86%]	6	[70%, 71%]
Internist	5	[89%, 91%]	5	[89%, 91%]	6	[74%, 75%]	6	[74%, 75%]
Consult OC	5	[88%, 89%]	5	[88%, 89%]	6	[73%, 74%]	6	[73%, 74%]
SNP	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]
POS	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]
SNI	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]	2	[45%, 47%]
Service level	[40%, 54%]		[55%, 63%]		[66%, 72%]		[81%, 86%]	
Average utilisation	84%		83%		80%		73%	
Average throughput time (in days)	[17.5, 24.5]		[15.5, 17.0]		[13.9, 14.6]		[12.2, 12.8]	

6.2.6 Scenario 5

For Scenario 5, two configurations perform best (see Table 15) and both require one time slot more than is suggested by the approximation model (see Appendix I for the results of the queuing model). As was discussed in 6.2.5, we prefer one additional time slot for ultrasonography over CRX. Therefore, we prefer experiment S5.2. Three time slots for either the ECG or NP2 result in an insufficient service level. When all patients require biopsy, we prefer experiment S5.3, where one additional time slot for chemotherapy is required instead of the MRI scan. Experiments S5.5 and S5.6 show that high utilisation for the four scarce appointments results in low service levels. The utilisation is not feasible to be increased as demand will exceed capacity.

Table 15: Results for Scenario 5

Scenario 5 (- 20% arrivals)	Normal settings				100% Biopsy				High utilisation			
Experiment (#)	S5.1		S5.2		S5.3		S5.4		S5.5		S5.6	
NP1	5	[52%, 53%]	5	[52%, 53%]	5	[52%, 53%]	5	[52%, 53%]	5	[52%, 53%]	5	[52%, 53%]
MRI	4	[56%, 58%]	4	[56%, 58%]	3	[74%, 77%]	4	[56%, 58%]	3	[74%, 77%]	3	[74%, 77%]
PET	4	[56%, 57%]	4	[56%, 57%]	4	[56%, 57%]	4	[56%, 57%]	3	[74%, 76%]	3	[74%, 76%]
EF	4	[62%, 64%]	4	[62%, 64%]	4	[62%, 64%]	4	[62%, 64%]	3	[83%, 86%]	4	[62%, 64%]
Biopsy	4	[46%, 47%]	4	[46%, 47%]	5	[54%, 56%]	5	[54%, 56%]	4	[46%, 47%]	4	[46%, 47%]
Chemotherapy	4	[62%, 64%]	4	[62%, 64%]	5	[50%, 51%]	4	[62%, 64%]	4	[62%, 64%]	4	[62%, 64%]
ECG	4	[56%, 58%]	4	[56%, 58%]	4	[56%, 58%]	4	[56%, 58%]	4	[56%, 58%]	4	[56%, 58%]
Ultrasonography Breast	3	[72%, 74%]	4	[54%, 56%]	4	[54%, 56%]	4	[54%, 56%]	4	[54%, 56%]	4	[54%, 56%]
CRX	4	[55%, 56%]	3	[73%, 75%]	4	[55%, 56%]	4	[55%, 56%]	4	[55%, 56%]	4	[55%, 56%]
NP2	4	[56%, 57%]	4	[56%, 57%]	4	[56%, 57%]	4	[56%, 57%]	4	[56%, 57%]	4	[56%, 57%]
Internist	4	[59%, 60%]	4	[59%, 60%]	4	[59%, 61%]	4	[59%, 60%]	3	[78%, 81%]	3	[78%, 81%]
Consult OC	4	[58%, 60%]	4	[58%, 60%]	4	[58%, 60%]	4	[58%, 60%]	4	[58%, 60%]	4	[58%, 60%]
SNP	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]
POS	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]
SNI	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]	2	[24%, 25%]
Service level	[90%, 94%]		[90%, 94%]		[90%, 93%]		[91%, 94%]		[68%, 76%]		[72%, 79%]	
Average utilisation	58%		58%		58%		58%		63%		62%	
Average throughput time (in days)	[11.4, 11.8]		[11.4, 11.9]		[12.1, 12.4]		[12.3, 12.7]		[13.7, 15.4]		[13.2, 14.3]	

6.2.7 Number of appointments

The required capacity is approximated through the simulation of the care pathway for the six scenarios. As is described in the list of assumptions in Section 5.1, we assume that patients receives appointments according to the protocol.

Although the configurations result in different arrival distributions to the NCT phase, we assume the effect on the weekly average requested appointments is insignificant. For all scenarios, the preferred configurations with normal settings (see previous paragraphs) are simulated. Table 16 shows the 95%-confidence intervals for the average number of appointments requested per week.

Table 16: 95%-confidence interval for average weekly number of requested appointments

	Consult OC	Chemotherapy treatment	NP appointment	MRI scan	Internist appointment
Base scenario (current arrival rate)	[2.9, 3.0]	[28.2, 29.4]	[9.2, 9.7]	[4.4, 4.6]	[2.4, 2.5]
Scenario 1 (+ 5% arrivals)	[3.1, 3.2]	[29.5, 31.7]	[9.8, 10.4]	[4.7, 5.0]	[2.6, 2.7]
Scenario 2 (+ 10% arrivals)	[3.2, 3.3]	[30.7, 32.3]	[10.1, 10.6]	[4.8, 5.0]	[2.6, 2.8]
Scenario 3 (+ 20% arrivals)	[3.5, 3.6]	[33.9, 35.5]	[11.1, 11.6]	[5.3, 5.6]	[2.9, 3.0]
Scenario 4 (+ 50% arrivals)	[4.3, 4.5]	[42.4, 44.3]	[13.9, 14.5]	[6.7, 6.9]	[3.6, 3.8]
Scenario 5 (- 20% arrivals)	[2.3, 2.4]	[22.4, 24.2]	[7.3, 7.9]	[3.5, 3.8]	[1.9, 2.1]

Table 17 gives the requested capacity in more detail for the consults at the Outpatient Clinic and the treatments at the Outpatient clinic. As the length of one treatment differs for chemotherapy types, we analyse the requested capacity by approximating the average number of treatments per week, per chemotherapy type. See Appendix K for more details. We conclude that in the current situation approximately three consults are required per week. For treatments, this patient group requests approximately 85 hours per week which corresponds to almost two beds (bed capacity is nine hours/day).

Table 17: Average requested capacity Outpatient Clinic (per week)

	Base Scenario	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
Consult OC	2.9	3.1	3.2	3.5	4.4	2.4
Minutes	176	188	192	212	264	142
Hours	3	3	3	4	4	2
Chemotherapy treatment	28.8	30.6	31.5	34.7	43.4	23.3
Minutes	5120	5441	5605	6181	7721	4147
Hours	85	91	93	103	129	69
Beds	1.9	2.0	2.1	2.3	2.9	1.5

As the average number of requested appointments gives no information about the variation in the requested appointments, we present insight in the dispersion in Figure 20-24. For each appointment type within the NCT phase and the Review phase, the ratio of the weeks in which the number of available appointments is sufficient to meet demand is shown. For example, 30 available treatments is for approximately 60% of the weeks enough to satisfy demand in Scenario 5 (see Figure 21). It is clear that the number of requested appointments significantly varies. Increasing arrival rates show flatter graphs which indicate more variation. Figure 20 shows less smooth graphs than the other figures as time slots are used to model the consult at the Outpatient Clinic.

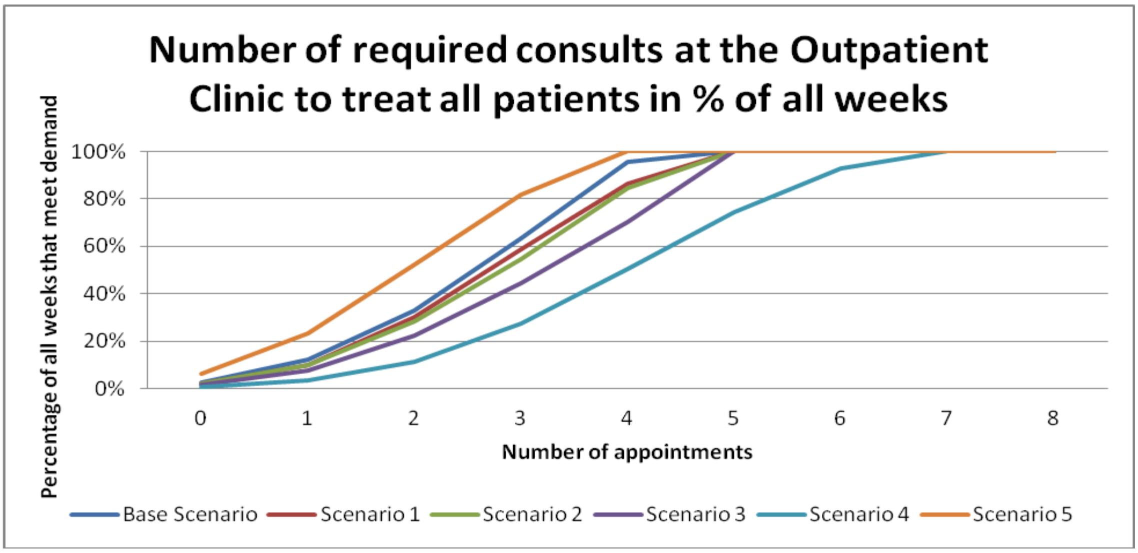

Figure 20: Number of consults at the Outpatient Clinic requested per week

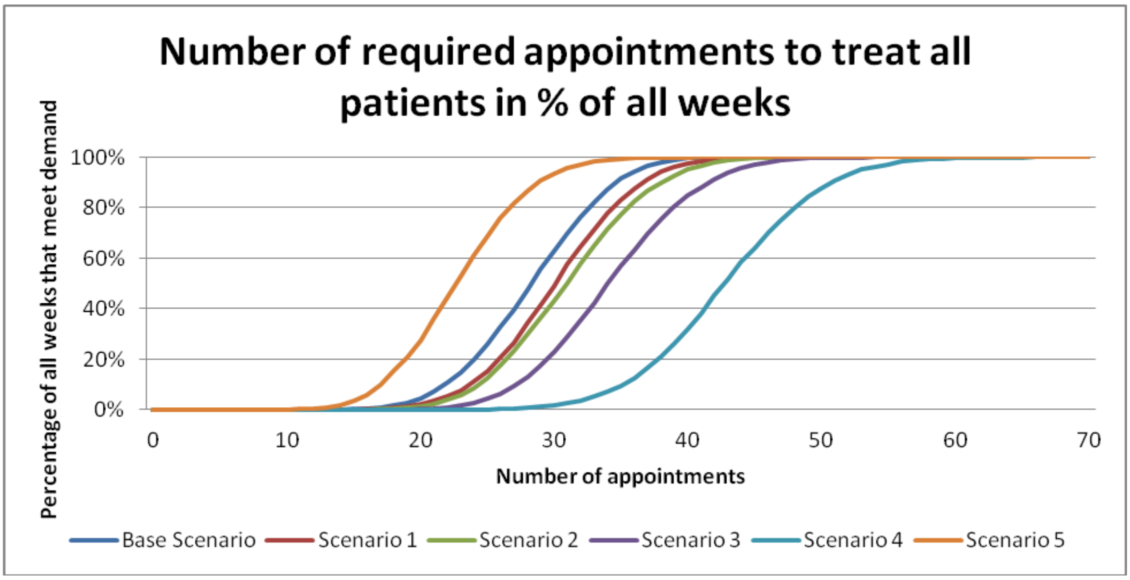

Figure 21: Number of treatments requested per week

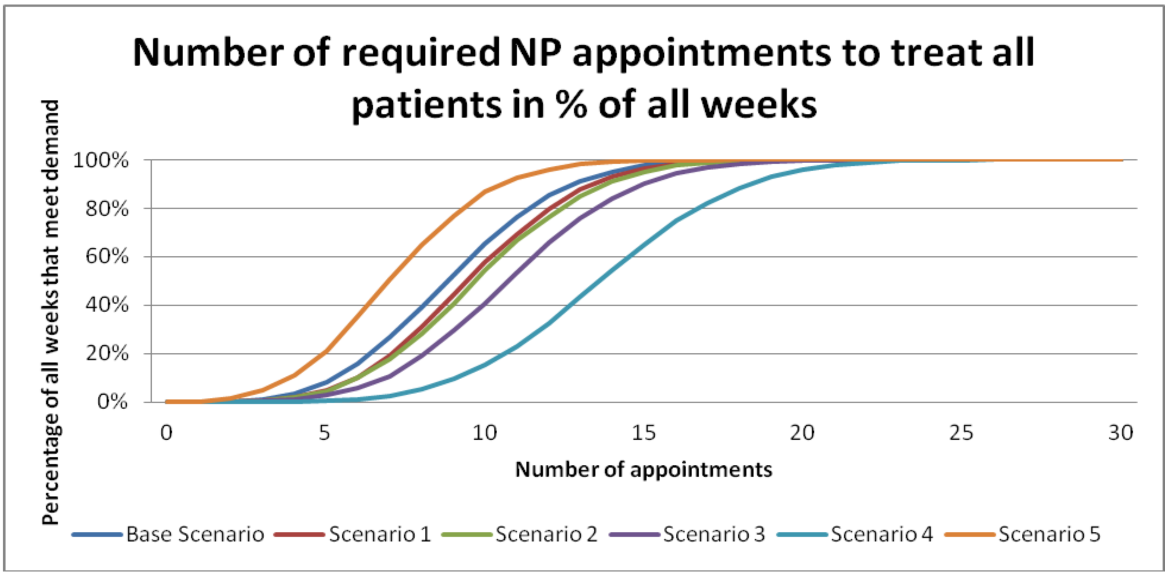

Figure 22: Number of NP appointments requested per week (during the NCT phase)

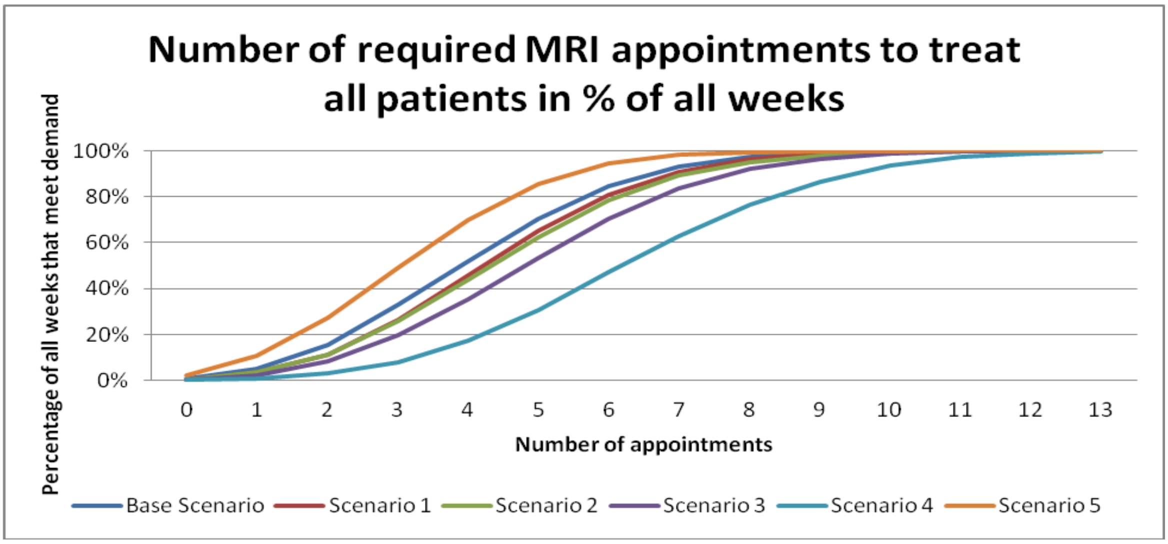

Figure 23: Number of MRI scans requested per week (during the NCT phase)

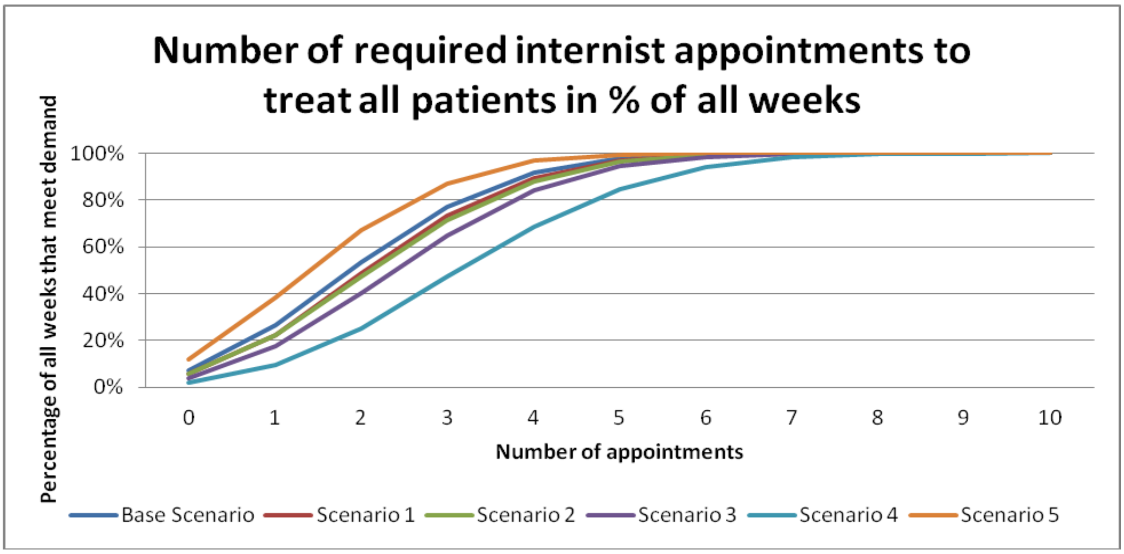

Figure 24: Number of internist appointments requested per week (during the NCT phase)

6.3 Discussion results

When scenarios are compared, we see increasing average utilisation of the time slots for increasing patient numbers (see Table 18). Thus, increase in arrivals suggests a positive effect on the utilisation of resources. For all standard appointments, the average utilisation for the Base Scenario is 65%. We see that especially the utilisation of time slots for the first NP appointment, biopsy, chemotherapy treatment and for the consult at the OC lower the average utilisation. Unfortunately, these appointments are all crucial appointments of which the impact on the throughput time of high utilisation is significant.

When comparing Scenario 1 with the Base Scenario we see that minor change in time slots results in the desired service level. One additional time slot for the appointment with the internist provides the same service level for 5% more arrivals. With three more time slots (for the MRI scan, chemotherapy and the internist appointment) the service level is regarded as sufficient for 10% more arrivals. For the default allocation of time slots, the number of hospital visits does not necessarily increase when more patients are assigned to this CP.

Table 18: Results of all scenarios

	Base Scenario	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
Required number of time slots	60	61	63	68	81	54
Required time slots (relative to Base Scenario)	-	102%	105%	113%	135%	90%
Average utilisation	65%	67%	68%	67%	70%	58%
Average number of visits	4.7	4.9	4.8	4.6	4.9	4.7

For the situation in which every patient requires the biopsy appointment, we see that for all scenarios (except Scenario 4) one or two additional time slots are sufficient, of which one should be for biopsy.

In order to achieve high utilisation of the time slots for the MRI scan, the EF, the PET/CT scan and the internist, we see that the service level significantly decreases and in most scenarios results in an insufficient service level. The impact of different utilisations is analysed. For non crucial appointments, a utilisation of around 70% yields in no significant (< 1%) percentage of patients required to wait longer than two weeks.

The allocation of time slots contributes significantly to the performance of the CP. Besides that time slots need to match the arrival distribution of patients, the alignment of the time slots with each other is important. Appointment scheduling restrictions highly affect appointment waiting times. An optimal schedule includes seven days between biopsy and internist appointment and another two until the first chemotherapy treatment. With a minimum throughput time of nine days, satisfying the desired service level is difficult when a patient arrives at Thursday and the biopsy cannot be performed before the weekend. The variation in delay which still satisfies the desired service level is limited. This also suggests that the biopsy appointment should be planned as quick as possible.

For utilisation of an arbitrary time slot, we see that utilisation over 80% results in a significant probability that an arbitrary appointment may not be planned within two weeks. For most appointments, waiting times of two weeks are not even feasible as other appointments are required to be planned subsequently. A strict maximum utilisation is difficult to determine, but we see that utilisations over 80% significantly affect the throughput time and decrease the service level. Furthermore, the probability of having to wait over two weeks is present for all utilisations. Even with a utilisation of 70%, we see a small percentage of the appointments (< 1%) not feasible to be planned within two weeks. As the CP contains a number of appointments, the probability that an arbitrary patient has at least one appointment with a waiting time over two weeks is obviously higher than for a single appointment. However, as not all patients receive each appointment and waiting times for individual appointments do not occur necessarily simultaneously nor apart from each other, the effect of the impact on the service level of multiple appointments is difficult to measure.

The preferred configurations for each scenario are shown in Table 19. The utilisation of the time slots for biopsy is relatively low in all scenarios. This is required since the biopsy appointment has great impact on the throughput time until the first chemotherapy treatment. For the scarce appointments, we conclude that high utilisations (> 80%) are not compatible with the desired service level when appointments are not allowed to be planned in overtime. Applying for the number of time slots calculated for the current situation might be unacceptable for the involved departments as utilisation is under 80%.

Table 19: Preferred configuration for each scenario

	Base Scenario		Scenario 1		Scenario 2		Scenario 3		Scenario 4		Scenario 5	
NP1	6	[54%, 55%]	6	[57%, 58%]	6	[60%, 61%]	6	[65%, 67%]	7	[70%, 71%]	5	[52%, 53%]
MRI	4	[70%, 72%]	4	[73%, 75%]	5	[62%, 63%]	5	[67%, 68%]	6	[70%, 71%]	4	[56%, 58%]
PET	4	[69%, 71%]	4	[73%, 75%]	4	[77%, 79%]	5	[67%, 68%]	6	[70%, 71%]	4	[56%, 57%]
EF	5	[62%, 64%]	5	[66%, 67%]	5	[69%, 71%]	5	[75%, 77%]	6	[78%, 80%]	4	[62%, 64%]
Biopsy	5	[45%, 47%]	5	[48%, 49%]	5	[50%, 52%]	5	[55%, 56%]	6	[57%, 59%]	4	[46%, 47%]
Chemotherapy	5	[62%, 64%]	5	[65%, 67%]	6	[57%, 58%]	6	[62%, 64%]	7	[67%, 68%]	4	[62%, 64%]
ECG	4	[70%, 72%]	4	[74%, 76%]	4	[78%, 80%]	5	[68%, 69%]	6	[71%, 72%]	4	[56%, 58%]
Ultrasonography Breast	4	[67%, 70%]	4	[71%, 73%]	4	[75%, 77%]	5	[65%, 67%]	6	[68%, 69%]	4	[54%, 56%]
CRX	4	[68%, 70%]	4	[72%, 74%]	4	[75%, 78%]	5	[66%, 68%]	5	[82%, 84%]	3	[73%, 75%]
NP2	4	[69%, 72%]	4	[73%, 75%]	4	[77%, 79%]	5	[67%, 69%]	6	[70%, 71%]	4	[56%, 57%]
Internist	4	[73%, 76%]	5	[62%, 63%]	5	[65%, 67%]	5	[71%, 72%]	7	[63%, 65%]	4	[59%, 60%]
Consult OC	5	[58%, 60%]	5	[61%, 63%]	5	[64%, 66%]	5	[70%, 72%]	7	[63%, 64%]	4	[58%, 60%]
SNP	2	[29%, 31%]	2	[31%, 33%]	2	[32%, 35%]	2	[35%, 38%]	2	[45%, 47%]	2	[24%, 25%]
POS	2	[29%, 31%]	2	[31%, 33%]	2	[32%, 35%]	2	[35%, 38%]	2	[45%, 47%]	2	[24%, 25%]
SNI	2	[29%, 31%]	2	[31%, 33%]	2	[32%, 35%]	2	[35%, 38%]	2	[45%, 47%]	2	[24%, 25%]
Service level	[90%, 94%]		[90%, 94%]		[90%, 94%]		[92%, 95%]		[90%, 93%]		[90%, 94%]	
Average utilisation	65%		67%		68%		67%		70%		58%	
Average throughput time (in days)	[11.4, 11.9]		[11.5, 11.8]		[11.3, 11.8]		[11.3, 11.6]		[11.3, 11.7]		[11.4, 11.9]	

Creating biweekly schedules instead of weekly schedules provides the opportunity to adjust the utilisation in more detail. For a number of appointment types in the Base Scenario, utilisation is either approximately 70% (with four time slots) or approximately over 90% (with three time slots). With biweekly schedules, three time slots are available in the odd weeks and four time slots in the even weeks. For these appointments, the utilisation is approximately 80%. However, with a utilisation of 80%, a significant part of the appointments cannot be planned within two weeks. With an average approximated utilisation of time slots for the ECG, ultrasonography, CRX and NP2 of 80%, the service level is a few percent below the desired service level. When the utilisation of all non crucial appointments is set to 80%, similar performance is observed with respect to the service level. See Appendix K for the results.

Although utilisations of 80% cause the service level to be less than 90%, it might be preferred as long as waiting times are avoided in reality through planning in overtime. This is mainly the case for consulting appointments such as both appointments with an NP and the appointment with an internist. For appointments related to resource equipment it is more difficult to work in overtime.

With respect to the appointments during the treatments, we see highly varying requested capacity. For chemotherapy treatments the average requested capacity is nearly two beds per week.

7 Conclusion and recommendations

This chapter presents the conclusion of this study in Section 7.1. The limitations of the results are also discussed. We present recommendations in Section 7.2.

7.1 Conclusion

This research tried to find the capacity necessary to be allocated to the neoadjuvant chemotherapy patients in order to start the chemotherapy treatment within two weeks for at least 90% of the regular patients. Moreover, we have analysed the course of treatments to assess the requested capacity.

In order to determine the required capacity for the desired service level, we applied the use of dedicated time slots for all appointments. Data analysis showed long waiting times for several appointments causing the throughput time to be too long. In particular, the availability of the PET/CT scan, EF and internist appointments showed a mismatch with moments the capacity is requested. Barely a fifth of the patients receive the first chemotherapy treatment within two weeks.

We used a combination of queuing theory and computer simulating to determine the required number of time slots in a number of arrival scenarios. Through a queuing model we approximated the required time slots which served as input for the simulation model. The performance of the configuration was analysed by means of a simulation model. We optimised the performance by experimenting with modifications in the time slot configuration. For the course of treatments, we approximated the average number of requested appointments.

Results show improved utilisation of time slots when more patients arrive. Nevertheless, utilisation is ought to be relatively low in order to start the treatment for at least 90% of the patients within two weeks. Literature study and queuing results showed the correlation between utilisation and waiting time. When utilisation increases, waiting time increases. Varying numbers of requested appointments per week require utilisation under 100% to be able to plan the appointments without outrageous waiting times. For an individual appointment, utilisation is limited to approximately 85% in order to plan at least 90% of the appointments within two weeks. Fixed sequencing between appointments makes this utilisation not feasible. With weekly schedules, the average utilisation of time slots for standard appointments is 65%. This is caused by two factors. First, since a fixed number of time slots is used to serve all patients, utilisation is either 65% (with four time slots/week) or over 85% (with three time slots/week). Simulation results showed that utilisation over 85% is not feasible with a desired service level of 90%, compelling the utilisation to be significant lower. Second, through appointment planning restrictions and sequencing of appointments, crucial appointments in the CP require even lower utilisation as the time period in which appointments can be planned is more limited. Biweekly schedules proved to enable more accurate alignment of capacity with demand, compared to weekly schedules. This is true since available capacity can be modified with one time slots per two weeks instead of one time slot per week.

Furthermore, the utilisation of time slots for the MRI scan, PET/CT scan, EF and internist appointment is analysed. The involved departments require high utilisation of time slots, since these capacities are considered to be scarce. However, the analysis showed that utilisation of these time slots is cannot be high (> 80%) while attaining a service level of 90%. Unfortunately, data analysis showed long waiting times for these appointments (except for the MRI scan) showing the necessity of time slots. So, in order to attain the desired service level, either moderate utilisation of the time slots has to be accepted or time slots should not be included. If the service level is relaxed, higher utilisations are attainable. As will be discussed in the following section, we suggest to decrease waiting time for these appointments regardless of the inclusion of time slots.

Moreover, it is vital to align the time slots with the moments the appointments are requested. As a vast majority of the patients (> 85%) enter the CP on Monday and Thursday afternoons, time slots allocation should be based on the arrival distribution. It is important that the biopsy time slots are appropriately scheduled, allowing the appointments to be planned as soon as possible. Six biopsy time slots are currently assigned to this patient group. The experiments showed that this number can be reduced, when appropriately allocated.

Finally, the analysis showed that the number of requested treatments per week vary significant. This is caused by the fluctuating arrival rate and the differences in treatment regimens.

Limitations

This study comes with a number of limitations. First, patient preferences are ignored. In reality patients desire to be seen at different days than proposed. Besides, the number of hospital visits is not regarded as relevant. A significant part of the patients do not live near the hospital or do not wish to visit the hospital for a single pre-assessment like the ECG. However, in order to create structured appointment schedules most appointments were scheduled at days other appointments are scheduled as well. This resulted in a limited number of hospital visits (approximately 4.7 visits for current arrivals). Moreover, the allocation of time slots is based on regular working hours.

Furthermore, since the inclusion of time slots requires more capacity than used, the availability of capacity for other patient groups decreases. For a number of appointments this is probably negligible as current capacity utilisation is rather low. Unfortunately, for a number of appointments such as the PET/CT scan and the EF, the utilisation is currently high. For these appointments, waiting times for other patient groups increase with the assignment of the time slots. However, time slots can be released. This is already applied in other CPs in the hospital. This approach creates available capacity for other patient groups as they are allowed to use the time slots initially assigned to the neoadjuvant chemotherapy patients.

In the simulation model, all patients are served during dedicated time slots and thus no overtime is allowed. However, it is unlikely that waiting times are unbounded. If, for example, the next available EF time slot is four weeks from now, the appointment is most likely to be planned outside the dedicated time slots (e.g. in overtime). With this approach, the utilisation of the time slots decreases as less appointments are planned in the time slots. Furthermore, the service level increases for two reasons. First, the throughput times of the involved patients decrease as service is earlier available. Second, the time slot which should be filled will be available for other patients.

Finally, the protocol regarding the chemotherapy treatments is recently modified and not included in our research. A new study is included with different treatment durations. Durations are significantly longer than in the observed situation, making the forecast with respect to the bed occupancy underestimated.

7.2 Recommendations

This paragraph outlines a few recommendations. The recommendations are divided in suggestions for further research, further development and further implementation.

Suggestions for further research

At AVL, appointment durations, time slot utilisation, cancelled or postponed appointments and no shows are barely or even not registered. We suggested to recorded these characteristics to improve alignment of capacity with demand. As the capacity required by a patient group is not calculated, the number of time slots is not appropriately determined. However, time slots are yet in use with for example the MRI scan. Data analysis and performance measurement is suggested for other patient groups as well. In this way, capacity is not unnecessarily occupied when too many time slots are claimed.

For the appointments at the Nuclear Medicine department, improvement of the current situation is recommended. The waiting times for the PET/CT scan and EF are significantly high and cause the desired service level to be unattainable when time slots are not included. Furthermore, research should indicate whether the current capacity is sufficient to serve all patients. More working hours, appointments in weekends or even additional capacity might be necessary. Moreover, considering prioritisation of patients is recommended. High numbers of appointments for research purposes are planned in short periods of time. This causes variability in utilisation and thus in waiting times for appointments.

Suggestions for further development

The inclusion of dedicated time slots should be further researched. Other patient groups should also be considered since their performance is affected by the introduction of time slots. Furthermore, the practice of releasing time slots and planning appointments outside the dedicated time slots should be examined. With both concepts, utilisation can be increased. When capacity is released, rather low utilisation of the time slots by this patient group is acceptable. This approach is already applied in other CPs in AVL. The impact on utilisation and the extent to which the released capacity is filled determine the success of this approach. With the possibility to plan patients outside the dedicated time slots, long waiting times are reduces. As only a small percentage of the appointments cannot be planned within two weeks with a utilisation of approximately 80%, these appointments might be executed in overtime. This is in particular applicable for consults like the appointments with NPs and internists where work in overtime is less complicated to realise than for resource equipment. The impact of allowing appointments in overtime and the relating penalties should be further researched. In addition, the impact on utilisation of time slots should be considered.

Suggestions for implementation

As the biopsy has a major impact on the throughput time, we suggest to plan this appointment at the day of arrival. Since six time slots are already in use for these appointments, we suggest to reallocate the capacity to Monday and Thursday afternoon. The allocation of time slots for the MRI scan should also be redesigned, matching the biopsy time slots. As the consult at the Outpatient Clinic as well as the first chemotherapy treatment depend on the appointment with the internist, it is important to align these time slots with biopsy. Therefore, the appointment with the internist should be scheduled exactly one week after the biopsy appointment. In this way, the Pathology department has sufficient time to report the results.

We see that time slot utilisations associated with the desired service level are relatively low (average utilisation is approximately 65%). When the desired service level is relaxed to for example 80% instead of 90%, we see that utilisation of half of the appointment types including the PET/CT scan and EF is allowed to increase to approximately 80%. Besides, when the requested throughput time is three weeks instead of two (as is included in national guidelines), time slots would be more effective as utilisation will be higher. Whether the desired service level is strictly necessary should be contemplated.

References

Andradottir, S. (1998). *A review of simulation optimization techniques*.

Azari-Rad, S., Yontef, A., Aleman, D. M., & Urbach, D. R. (2014). A simulation model for perioperative process improvement. *Operations Research for Health Care, 3*(1), 22-30.

Benneyan, J. C. (1997). An introduction to using computer simulation in healthcare: patient wait case study. *Journal of the Society for Health Systems, 5*(3), 1-15.

Berry, D. M. (2013). The essential similarity and differences between mathematical modeling and programming. *Science of Computer Programming, 78*(9), 1208-1211.

Blake, J. T. D. J. (2002). Mount Sinai Hospital Uses Integer Programming to Allocate Operating Room Time. [Article]. *Interfaces, 32*(2), 63-73.

Cardoen, B., & Demeulemeester, E. (2007). Evaluating the capacity of clinical pathways through discrete-event simulation. FETEW Research Report KBI_0712, Katholieke Universiteit Leuven, Department of Decision Sciences and Information Management.

Du, G., Jiang, Z., Yao, Y., & Diao, X. (2013). Clinical Pathways Scheduling Using Hybrid Genetic Algorithm. *Journal of Medical Systems, 37*(3), 1-17.

Fenwick, P. (2002). Queueing Theory. 1-21.

Filipowicz, B., & Kwiencien, J. (2008). Queueing systems and networks. Models and applications. *Bulletin Of The Polish Academy Of Sciences-technical Sciences, 56*(4), 379-390.

Gross, D., Shortle, J. F., Thompson, J. M., & Harris, C. M. (2008). Fundamentals of Queuing Theory.

Hall, R. W. (2006). Patient Flow: Reducing Delay in Healthcare Delivery.

Hans, E. W., Van Woudenhoven, M., & Hulshof, P. J. H. (2011). A framework for health care planning and control. 1-23.

Hulshof, P. J. H., Kortbeek, N., Boucherie, R. J., Hans, E. W., & Bakker, P. J. M. (2012). Taxonomic classification of planning decisions in health care: a structured review of the state of the art in OR/MS. *Health Systems, 1*(2), 129-175.

Hummel, H., Otter, R., & de Vries, J. (2010). Integrale oncologische zorgpaden: van model naar 'daily practice'. 1-139.

IBM. SPSS Statistics *22*.

Jaardocument 2012 Antoni van Leeuwenhoek. (2013).

Jacobson, S., Hall, S., & Swisher, J. (2006). Discrete-Event Simulation of Health Care Systems. In R. Hall (Ed.), *Patient Flow: Reducing Delay in Healthcare Delivery* (Vol. 91, pp. 211-252): Springer US.

Jiang, L., & Giachetti, R. (2008). A queueing network model to analyze the impact of parallelization of care on patient cycle time. *Health Care Management Science, 11*(3), 248-261.

Kapadia, A. S., Vineberg, S. E., & Rossi, C. D. (1985). Predicting course of treatment in a rehabilitation hospital: A Markovian model. *Computers & Operations Research, 12*(5), 459-469.

Kolisch, R., & Sickinger, S. (2008). Providing radiology health care services to stochastic demand of different customer classes. *OR Spectrum, 30*(2), 375-395.

Kuip, C. A. C. (1993). Algebraic languages for mathematical programming. *European Journal of Operational Research, 67*(1), 25-51.

Kwak, N. K., & Lee, C. (1997). A Linear Goal Programming Model for Human Resource Allocation in a Health-Care Organization. *Journal of Medical Systems, 21*(3), 129-140.

Law, A. M. (2007). Simulation modeling and analysis. [Book]. (4), McGraw-Hill.

Liyanage, L., & Gale, M. (1995, 22-25 Oct 1995). *Quality improvement for the Campbelltown hospital emergency service.* Paper presented at the Systems, Man and Cybernetics, 1995. Intelligent Systems for the 21st Century., IEEE International Conference on.

Mardiah, F. P., & Basri, M. H. (2013). The Analysis of Appointment System to Reduce Outpatient Waiting Time at Indonesia's Public Hospital. *Human Resource Management Research, 3*(1), 27-33.

Maull, R. S., Smart, P. A., Harris, A., & Karasneh, A. A.-F. (2009). An evaluation of 'fast track' in A&E: a discrete event simulation approach. *The Service Industries Journal, 29*(7), 923-941.

McClean, S., & Millard, P. (1998). A three compartment model of the patient flows in a geriatric department: a decision support approach. *Health Care Management Science, 1*(2), 159-163.

Breast cancer: Dutch Guideline. NABON. (2012). (version 2.0), 1-214.

Nunes, L. G. N., de Carvalho, S. V., & Rodrigues, R. d. C. M. (2009). Markov decision process applied to the control of hospital elective admissions. *Artificial Intelligence in Medicine, 47*(2), 159-171.

Olafsson, S. (2006). Metaheuristics. *Handbook in Operations Research and Management Science VII*, 633-654.

Siemens. Technomatix Plant Simulation 10.1.

Smith, K. R., Jr, A. M. O., Hansen, M. F., Golladay, F. L., & Davenport, E. J. (1976). Analytic Framework and Measurement Strategy for Investigating Optimal Staffing in Medical Practice. *Operations Research, 24*(5), 815-841.

Thomas, S. J., Williams, M. V., Burnet, N. G., & Baker, C. R. (2001). How Much Surplus Capacity is Required to Maintain Low Waiting Times? *Clinical Oncology, 13*(1), 24-28.

van Vliet, E. J., Sermeus, W., van Gaalen, C. M., Sol, J. C. A., & Vissers, J. M. H. (2010). Efficacy and efficiency of a lean cataract pathway: a comparative study. *Quality and Safety in Health Care, 19*(6), 1-6.

Vanhaecht, K., & Sermeus, W. (2003). The Leuven Clinical Pathway Compass. *Journal of Integrated Pathways, 7*(1), 2-7.

Vermeulen, I. B., Bohte, S. M., Elkhuizen, S. G., Lameris, H., Bakker, P. J. M., & Poutré, H. L. (2009). Adaptive resource allocation for efficient patient scheduling. *Artificial Intelligence in Medicine, 46*(1), 67-80.

White Iii, C. C., & White, D. J. (1989). Markov decision processes. *European Journal of Operational Research, 39*(1), 1-16.

Winston, W. L. (2004). Operations Research: Applications and Algorithms.

Zeng, Z., Ma, X., Hu, Y., Li, J., & Bryant, D. (2012). A Simulation Study to Improve Quality of Care in the Emergency Department of a Community Hospital. *Journal of Emergency Nursing, 38*(4), 322-328.

Zijm, W. H. M. (2003). Manufacturing and logistic systems analysis, planning and control. [Lecture notes]. 1-106.

Appendices

Appendix A: Appointments in the Additional Tests and Pre-assessment (ATP) phase

Table 1: Appointment restrictions (ATP phase)

Appointment	Restrictions	Department	Standard appointment?	Results after?
NP (nurse practitioner)	First appointment: First appointment in the ATP phase Second appointment: None	Internal Medicine	Yes	-
CXR (chest X-ray)	None	Radiology	Yes	directly
Ultrasonography Breast	Dedicated time slots	Radiology	Yes	directly
Biopsy	Dedicated time slots	Radiology	Yes	5 days
MRI scan	Not within five days after the biopsy; dedicated time slots	Radiology	Yes	2 days
PET/CT scan	If on the same day as the EF: first the EF and then PET/CT scan If on the same day as radiological examinations: first the radiological examinations, then PET/CT scan	Nuclear Medicine	Yes	1 day
EF (Ejection Fraction)	See PET/CT. If on the same day as radiological examinations: first the radiological examinations, then EF	Nuclear Medicine	Yes	1 day
ECG	None	Anaesthesia	Yes	directly
POS (preoperative screening)	See SNI	Anaesthesia	No	-
SNI (sentinel node imaging)	After POS	Nuclear Medicine	No	directly
SNP (sentinel node procedure)	After SNI	OR theatre	No	-
Internist	After all results of pathology are reported	Internal Medicine	Yes	-
Consultation outpatient clinic	After appointment with the internist	Outpatient clinic	Yes	-

Appendix B: Chemotherapy Treatments

Patients start with one of two chemotherapy types, knowing AC and PTC (which are abbreviations of the involved drugs). The selection depends on the HER2/neu protein. In case of an unfavourable response measurement after the first treatment cycle, patients switch to Paclitaxel or FEC, respectively after AC or PTC, as shown in Table 2 on the next page.

Appointments with an NP are scheduled prior to chemotherapy treatments to monitor the physical condition of the patient, clarify the current plan of action and assist patients during this phase. Prior to every treatment, the patients' blood is evaluated. Chemotherapy will not be dosed (at that particular day) if the blood values are considered inappropriate. A missed treatment is postponed or cancelled, depending on the chemotherapy type. Since appointment planning is not applicable with blood testing (patients arrive on walk-in basis), these events are not covered in this thesis.

Between cycles are time intervals in which no treatment is dosed. The patients' response to the chemotherapy treatment is evaluated during the time interval after the first cycle. An MRI scan monitors the tumour. This image is compared with the previous MRI scan during an MDT deliberation to obtain differences in tumour size. The team subsequently decides which chemotherapy type is used for the remaining treatments. Either the same chemotherapy type, or another chemotherapy type is dosed. The former is dosed when sufficient reduction in tumour size is perceived while the latter is dosed when this is not the case. The internist discusses the result with the patients after which they start with the second treatment cycle. A third treatment cycle is include for the chemotherapy type PTC.

Aside from the appointments associated with the treatment, patients who satisfy specific characteristics are requested to voluntarily participate in the PET/CT scan study. Involved patients have two additional PET/CT scans during the NCT phase for research purposes. The rest of the care pathway remains unaffected.

Appointments during the NCT phase (apart from the first treatment) are planned once the first chemotherapy treatment is dosed.

Table 2: Chemotherapy type characteristics

	AC	Paclitaxel	PTC	FEC
Total number of treatments	6	9	18	4
Number of cycles	2	1	3	1
Interval between two treatments	2 weeks	1 week	1 week	3 weeks
Interval between two cycles	2 weeks	-	3 weeks	-
NP (before treatment #)	2, 3, 5, 6	4, 7	4, 10, 13, 16	2, 3, 4
Switch to type if unfavourable	Paclitaxel	-	FEC	-
Treatment not received?	postponed	cancelled	cancelled	postponed
PET/CT scan for research (before treatment #)	2, 4	-	4, 7	-

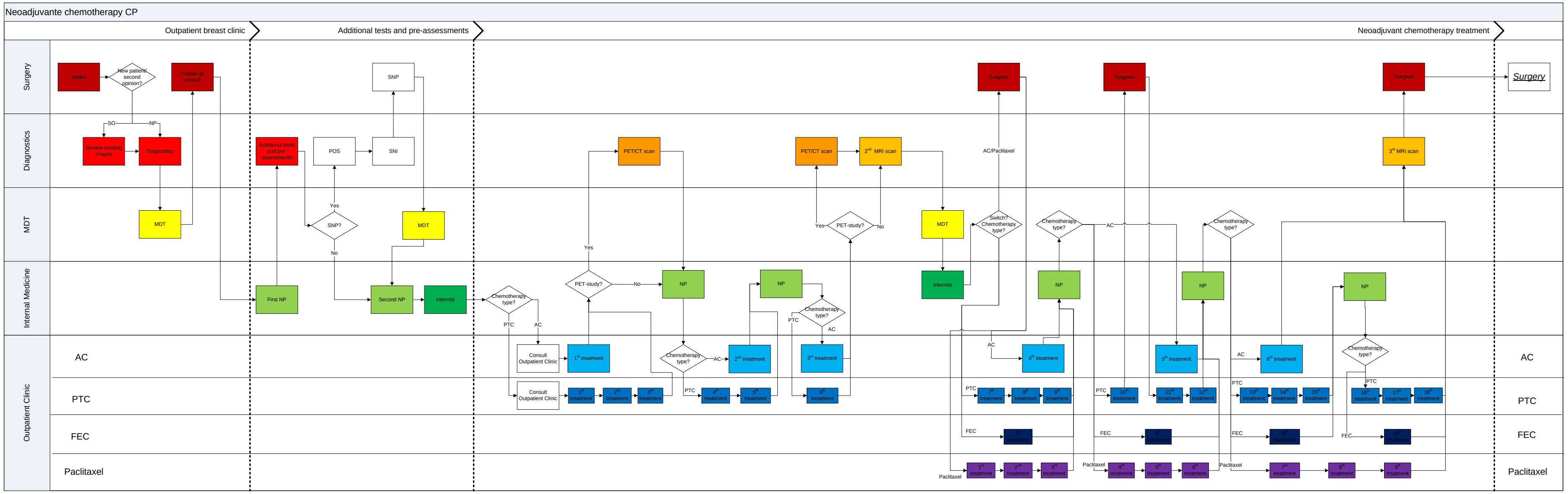

Figure 1: Flowchart of the neoadjuvant chemotherapy CP

Appendix C: Performance indicators

Table 3: Throughput time from the biopsy appointment date until the appointment with an internist (in days)

	Total # appointments	Average throughput time	Standard deviation	5th percentile	25th percentile	50th percentile	75th percentile	95th percentile
Biopsy date - internist appointment	95	10.46	2.89	7	8	10	13	16

Table 4: Chemotherapy types: percentage of the patients travelling a specific route (patients who have not finished the CP at the moment of data recording were excluded)

Indicator	2012	2013	Total
a) Chemotherapy	92%	91%	91%
b) Chemotherapy type AC	73%	70%	71%
c) Chemotherapy type AC (favourable response)	76%	81%	79%
d) Chemotherapy type AC (switch to other type)	24%	19%	21%
e) Chemotherapy type PTC	17%	26%	22%
f) Chemotherapy type PTC (favourable response)	100%	92%	94%
g) Chemotherapy type PTC (switch to other type)	0%	9%	6%

Appendix D: Analysis of the Arrival Distribution

Output SPSS with a one-sample Kolmogorov-Smirnov test for weekly arrivals.

Table 5: SPSS output (weekly arrivals)

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
ArrivalsTotal	98	3.4490	2.03638	.00	10.00	2.0000	3.0000	4.2500

One-Sample Kolmogorov-Smirnov Test

		ArrivalsTotal
N		98
Poisson Parameter[a,b]	Mean	3.4490
Most Extreme Differences	Absolute	.047
	Positive	.047
	Negative	-.041
Kolmogorov-Smirnov Z		.467
Asymp. Sig. (2-tailed)		.981

a. Test distribution is Poisson.

b. Calculated from data.

Output SPSS with a one-sample Kolmogorov-Smirnov test for daily arrivals.

Table 6: SPSS output (daily arrivals)

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
ArrivalsMondayTotal	98	1.3673	1.18746	.00	5.00	.7500	1.0000	2.0000
ArrivalsTuesdayTotal	98	.1633	.39829	.00	2.00	.0000	.0000	.0000
ArrivalsWednesdayTotal	98	.1939	.42251	.00	2.00	.0000	.0000	.0000
ArrivalsThursdayTotal	98	1.6020	1.25788	.00	7.00	1.0000	1.0000	2.2500
ArrivalsFridayTotal	98	.1327	.36995	.00	2.00	.0000	.0000	.0000

One-Sample Kolmogorov-Smirnov Test

		ArrivalsMondayTotal	ArrivalsTuesdayTotal	ArrivalsWednesdayTotal	ArrivalsThursdayTotal	ArrivalsFridayTotal
N		98	98	98	98	98
Poisson Parameter[a,b]	Mean	1.3673	.1633	.1939	1.6020	.1327
Most Extreme Differences	Absolute	.040	.002	.007	.038	.002
	Positive	.040	.002	.006	.038	.002
	Negative	-.025	-.002	-.007	-.028	-.002
Kolmogorov-Smirnov Z		.393	.024	.074	.379	.021
Asymp. Sig. (2-tailed)		.998	1.000	1.000	.999	1.000

a. Test distribution is Poisson.

b. Calculated from data.

Appendix E: Queuing Results for Scenario 1-5

Table 7: Queuing results for Scenario 1-5

Scenario	Arrivals + 5%		Arrivals + 10%		Arrivals + 20%		Arrivals + 50%		Arrivals - 20%	
Appointment type	Input parameter	Output parameter	Input parameter	Output parameter	Input parameter	Output parameter	Input parameter	Output parameter	Input parameter	Output parameter
Node i	Arrival rate λ_i	Service rate μ_i (integer)	Arrival rate λ_i	Service rate μ_i (integer)	Arrival rate λ_i	Service rate μ_i (integer)	Arrival rate λ_i	Service rate μ_i (integer)	Arrival rate λ_i	Service rate μ_i (integer)
1. 1st NP	3.47	5	3.63	5	3.96	5	4.95	7	2.64	4
2. Biopsy	2.49	4	2.61	4	2.84	4	3.56	5	1.90	3
3. MRI scan	2.97	4	3.11	5	3.40	5	4.25	6	2.26	4
4. ECG	3.10	5	3.25	5	3.54	5	4.43	6	2.36	4
5. PET/CT scan	2.99	4	3.14	5	3.42	5	4.28	6	2.28	4
6. EF	3.34	5	3.50	5	3.82	5	4.77	6	2.54	4
7. Ultrasono-graphy breast	2.96	4	3.10	5	3.38	5	4.23	6	2.26	4
8. CRX	2.92	4	3.06	5	3.34	5	4.17	6	2.22	4
9. 2nd NP	2.99	4	3.14	5	3.42	5	4.28	6	2.28	4
10. SNP	0.62	2	0.65	2	0.71	2	0.89	2	0.47	2
11. Internist	3.05	5	3.19	5	3.48	5	4.35	6	2.32	4
12. Consult OC	3.03	5	3.18	5	3.47	5	4.34	6	2.31	4
13. 1st chemo-therapy treatment	3.20	5	3.36	5	3.66	5	4.58	6	2.44	4

Appendix F: Appointment Planning Restrictions

- Appointment with an NP is the first appointment in the process
- Biopsy is performed after the MRI scan or MRI scan is performed at least five days after the biopsy
- The results of the MRI scan are known two days after the appointment
- The results of the PET/CT scan are known one day after the appointment
- Appointment with an internist is performed at least x days after the biopsy (with x as an input parameter)
- Appointment with an internist is performed after ECG, MRI, PET/CT, EF, Ultrasonography Breast, X-ray and NP2
- If on the same day: PET/CT scan is performed after the EF
- If on the same day as radiological examinations: first radiological examinations, then EF
- If on the same day as radiological examinations: first radiological examinations, then PET/CT scan
- SN is performed after the results of the PET/CT scan and the biopsy are reported [default settings: PET/CT = 1 day; biopsy = 5 days]
- Consultation appointment at the outpatient clinic is performed after all other standard appointments (excluding the neoadjuvant chemotherapy treatment)
- The first chemotherapy treatment is performed after all standard appointments and SN are performed and not on the same day as the SN

Appendix G: Appointment Probabilities

Table 8: Appointment probabilities (ATP phase and first chemotherapy treatment)

	Prob NP	Prob MRI	Prob PET	Prob EF	Prob Biopsy	Prob Chemotherapy	Prob ECG	Prob Ultrasonography Breast
Regular patients	0.95	0.84	0.86	0.97	0.71	1.00	0.87	0.83
No chemo patients	1.00	0.62	0.41	0.41	0.31	0.00	0.41	0.48

	Prob Xray	Prob NP2	Prob Internist	Prob ConsultOD	Prob SN	Prob AC	Prob PTC
Regular patients	0.83	0.85	0.95	0.92	0.19	0.76	0.24
No chemo patients	0.52	0.55	0.00	0.17	0.00	0.00	0.00

Table 9: Appointment probabilities (NCT phase)

	Prob 2	Prob 3	Prob 4	Prob 5	Prob 6	Prob 7	Prob 8	Prob 9	Prob 10
AC	0.98	0.99	0.76	0.95	0.91	0	0	0	0
AC switch Taxol	-	-	0.22	1	1	1	1	0.92	1
PTC	1	1	1	1	1	0.94	1	1	1
PTC switch FEC	-	-	-	-	-	0.06	1	1	1

	Prob 11	Prob 12	Prob 13	Prob 14	Prob 15	Prob 16	Prob 17	Prob 18
AC	0	0	0	0	0	0	0	0
AC switch Taxol	0.91	0.9	0	0	0	0	0	0
PTC	1	0.98	0.98	0.98	0.94	0.98	0.98	0.95
PTC switch FEC	0	0	0	0	0	0	0	0

Appendix H: Appointment Durations

Table 10: Appointment durations

Appointment type	Appointment duration (in minutes)
1st appointment NP	45:00
Biopsy	10:00
MRI	30:00
ECG	10:00
PET/CT	120:00
EF	30:00
Ultrasonography breast (I-125)	10:00
X-ray	10:00
2nd appointment NP	45:00
Preoperative screening	20:00
SN imaging	240:00
SN scintigraphy	120:00
Internist	45:00
Consult outpatient clinic	60:00
Chemotherapy treatment	90:00

Appendix I: Time Slot Schedules

Appoint-ment Type	Time slot number	Day of the week	Time	Appoint-ment Type	Time slot number	Day of the week	Time	Appoint-ment Type	Time slot number	Day of the week	Time	Appointment Type	Time slot number	Day of the week	Time
NP1	1	Thursday	13:30:00	**MRI**	1	Thursday	15:00:00	**PET/CT**	1	Friday	14:00:00	**EF**	1	Friday	10:20:00
NP1	2	Monday	13:30:00	**MRI**	2	Monday	15:00:00	**PET/CT**	2	Tuesday	14:00:00	**EF**	2	Tuesday	10:20:00
NP1	3	Thursday	14:00:00	**MRI**	3	Thursday	15:30:00	**PET/CT**	3	Friday	14:30:00	**EF**	3	Friday	10:50:00
NP1	4	Monday	14:00:00	**MRI**	4	Monday	15:30:00	**PET/CT**	4	Tuesday	14:30:00	**EF**	4	Tuesday	10:50:00
NP1	5	Thursday	14:30:00	**MRI**	5	Thursday	16:00:00	**PET/CT**	5	Friday	15:00:00	**EF**	5	Friday	11:20:00
NP1	6	Monday	14:30:00	**MRI**	6	Monday	15:45:00	**PET/CT**	6	Tuesday	15:00:00	**EF**	6	Tuesday	11:20:00
NP1	7	Wednesday	13:30:00	**MRI**	7	Wednesday	15:00:00	**PET/CT**	7	Thursday	14:00:00	**EF**	7	Thursday	10:20:00
NP1	8	Wednesday	14:00:00	**MRI**	8	Wednesday	15:30:00	**PET/CT**	8	Thursday	14:30:00	**EF**	8	Thursday	10:50:00
NP1	9	Wednesday	14:30:00	**MRI**	9	Wednesday	16:00:00	**PET/CT**	9	Thursday	15:00:00	**EF**	9	Thursday	11:20:00

Appoint-ment Type	Time slot number	Day of the week	Time	Appoint-ment Type	Time slot number	Day of the week	Time	Appoint-ment Type	Time slot number	Day of the week	Time	Appointment Type	Time slot number	Day of the week	Time
CRX	1	Friday	09:00:00	**NP2**	1	Friday	12:00:00	**Internist**	1	Monday	08:30:00	**Consult OC**	1	Monday	
CRX	2	Tuesday	09:00:00	**NP2**	2	Tuesday	12:00:00	**Internist**	2	Thursday	08:30:00	**Consult OC**	2	Thursday	12:00:00
CRX	3	Friday	09:10:00	**NP2**	3	Friday	12:30:00	**Internist**	3	Monday	09:15:00	**Consult OC**	3	Monday	13:00:00
CRX	4	Tuesday	09:10:00	**NP2**	4	Tuesday	12:30:00	**Internist**	4	Thursday	09:15:00	**Consult OC**	4	Thursday	13:00:00
CRX	5	Friday	09:20:00	**NP2**	5	Friday	13:00:00	**Internist**	5	Monday	10:00:00	**Consult OC**	5	Monday	14:00:00
CRX	6	Tuesday	09:20:00	**NP2**	6	Tuesday	13:00:00	**Internist**	6	Thursday	10:00:00	**Consult OC**	6	Thursday	14:00:00
CRX	7	Thursday	09:00:00	**NP2**	7	Thursday	12:00:00	**Internist**	7	Wednesday	08:30:00	**Consult OC**	7	Wednesday	12:00:00
CRX	8	Thursday	09:10:00	**NP2**	8	Thursday	12:30:00	**Internist**	8	Wednesday	09:20:00	**Consult OC**	8	Wednesday	13:00:00
CRX	9	Thursday	09:20:00	**NP2**	9	Thursday	13:00:00	**Internist**	9	Wednesday	10:00:00	**Consult OC**	9	Wednesday	14:00:00

Appoint-ment Type	Time slot number	Day of the week	Time	Appoint-ment Type	Time slot number	Day of the week	Time	Appoint-ment Type	Time slot number	Day of the week	Time	Appointment Type	Time slot number	Day of the week	Time
Biopsy	1	Thursday	16:30:00	**Chemotherapy**	1	Monday	15:10:00	**ECG**	1	Friday	09:30:00	**Ultrasonography Breast**	1	Friday	08:30:00
Biopsy	2	Monday	16:30:00	**Chemotherapy**	2	Thursday	15:10:00	**ECG**	2	Tuesday	09:30:00	**Ultrasonography Breast**	2	Tuesday	08:30:00
Biopsy	3	Thursday	16:40:00	**Chemotherapy**	3	Monday	15:20:00	**ECG**	3	Friday	09:40:00	**Ultrasonography Breast**	3	Friday	08:40:00
Biopsy	4	Monday	16:40:00	**Chemotherapy**	4	Thursday	15:20:00	**ECG**	4	Tuesday	09:40:00	**Ultrasonography Breast**	4	Tuesday	08:40:00
Biopsy	5	Thursday	16:50:00	**Chemotherapy**	5	Monday	15:30:00	**ECG**	5	Friday	09:50:00	**Ultrasonography Breast**	5	Friday	08:50:00
Biopsy	6	Monday	16:50:00	**Chemotherapy**	6	Thursday	15:30:00	**ECG**	6	Tuesday	09:50:00	**Ultrasonography Breast**	6	Tuesday	08:50:00
Biopsy	7	Wednesday	16:30:00	**Chemotherapy**	7	Wednesday	15:10:00	**ECG**	7	Thursday	09:30:00	**Ultrasonography Breast**	7	Thursday	08:30:00
Biopsy	8	Wednesday	16:40:00	**Chemotherapy**	8	Wednesday	15:20:00	**ECG**	8	Thursday	09:40:00	**Ultrasonography Breast**	8	Thursday	08:40:00
Biopsy	9	Wednesday	16:50:00	**Chemotherapy**	9	Wednesday	15:30:00	**ECG**	9	Thursday	09:50:00	**Ultrasonography Breast**	9	Thursday	08:50:00

Appoint-ment Type	Time slot number	Day of the week	Time	Appoint-ment Type	Time slot number	Day of the week	Time	Appointment Type	Time slot number	Day of the week	Time
SNP	1	Wednesday	15:00:00	**POS**	1	Wednesday	10:40:00	**SNI**	1	Wednesday	11:00:00
SNP	2	Friday	15:00:00	**POS**	2	Friday	10:40:00	**SNI**	2	Friday	11:00:00
SNP	3	Tuesday	15:00:00	**POS**	3	Tuesday	10:40:00	**SNI**	3	Tuesday	11:00:00

Appendix J: Warm-up Period

We calculated the warm-up period with the graphical procedure of Welch. For the first model, we choose the number of replications *n* to be 10, the window *w* to be 200 and the number of replications *m* to be 1040 (i.e. 20 years). For the second model, we choose the number of replications *n* to be 10, the window *w* to be 25 and the number of replications *m* to be 520 (i.e. 10 years). Figure 2 and Figure 3 show the graphical result of this approach for both objectives.

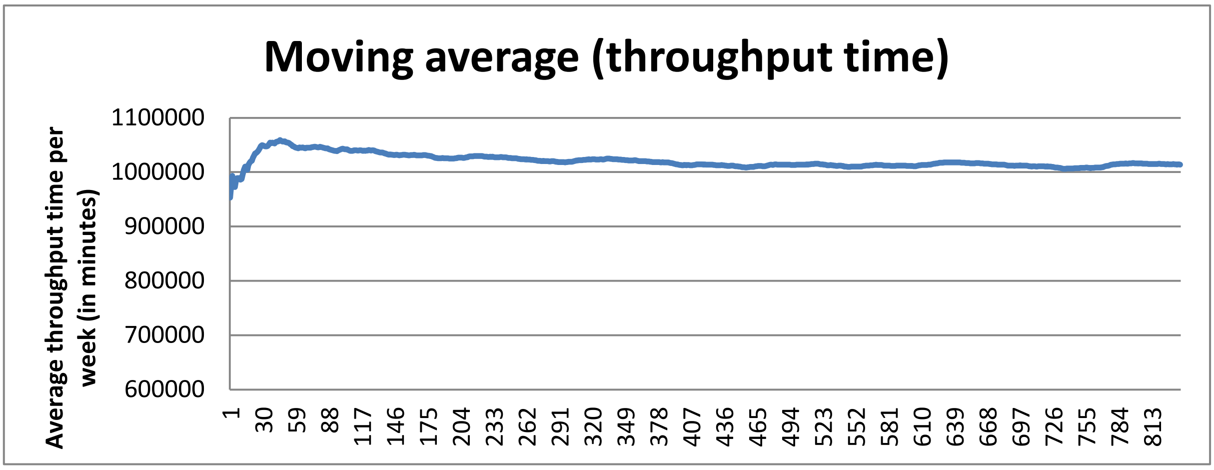

Figure 2: Warm-up period (objective 1)

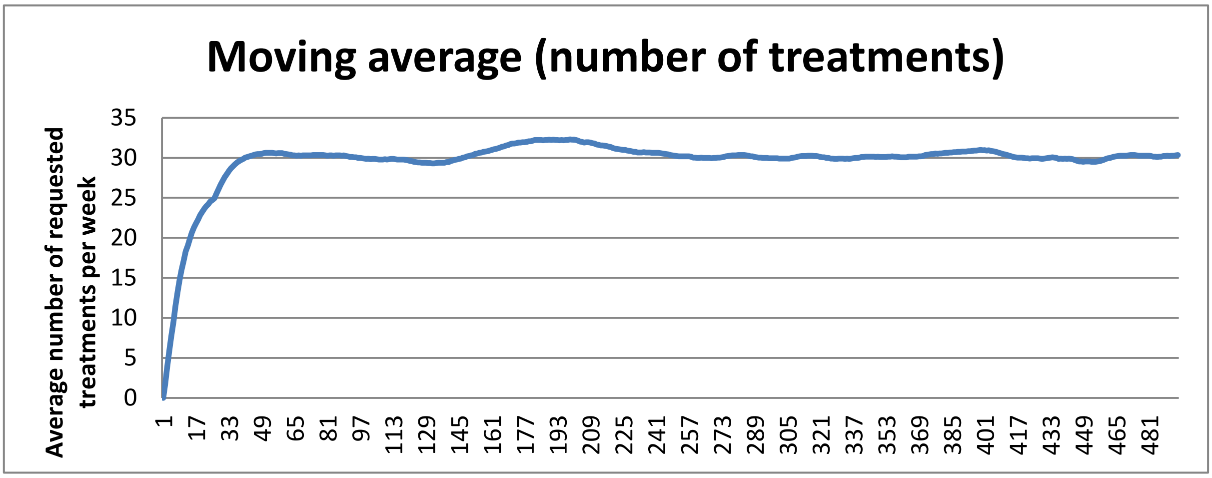

Figure 3: Warm-up period (objective 2)

Appendix K: Experimental results

Table 11: Factors (input parameters) and their level

Factor	Description	-	+
1	Number of time slots NP1	5	6
2	Number of time slots MRI	4	5
3	Number of time slots Biopsy	4	5
4	Number of time slots Internist	4	5
5	Number of time slots Consult OC	4	5
6	Number of time slots Chemotherapy	5	6
7	Number of time slots PET	4	5
8	Number of time slots EF	5	6
9	Number of time slots ECG	4	5
10	Number of time slots Ultrasonography Breast	4	5
11	Number of time slots CRX	4	5
12	Number of time slots NP2	4	5
13	Number of time slots POS/SNI/SNP	2	3

Table 12: Factorial design main effects on the average service level and interactions

Main effects		Two-way interactions		Three-way interactions	
e_1	1.55%	e_{12}	3.05%	e_{123}	5.26%
e_2	1.90%	e_{13}	4.04%	e_{124}	4.48%
e_3	2.54%	e_{14}	2.99%	e_{125}	4.07%
e_4	1.34%	e_{15}	2.65%	e_{126}	4.23%
e_5	0.96%	e_{16}	2.55%	e_{134}	5.78%
e_6	1.00%	e_{23}	4.34%	e_{135}	5.34%
e_7	0.03%	e_{24}	3.20%	e_{136}	4.65%
e_8	0.00%	e_{25}	2.83%	e_{145}	5.12%
e_9	0.03%	e_{26}	3.10%	e_{146}	4.28%
e_{10}	0.02%	e_{34}	4.13%	e_{156}	3.70%
e_{11}	0.03%	e_{35}	3.67%	e_{234}	5.83%
e_{12}	0.08%	e_{36}	3.10%	e_{235}	5.35%
e_{13}	0.00%	e_{45}	3.25%	e_{236}	5.00%
		e_{46}	2.63%	e_{245}	5.04%
		e_{56}	2.00%	e_{246}	4.65%
				e_{256}	4.08%
				e_{345}	6.10%
				e_{346}	5.03%
				e_{356}	4.33%
				e_{456}	4.66%

Table 13: Experimental results (Base Scenario)

Experiment	Queuing model	a	b	c	d	e	f	g	h	i
NP1	5	6	6	6	5	5	5	5	5	5
MRI	4	4	4	4	5	5	5	4	4	5
PET	4	4	4	4	4	4	4	4	4	4
EF	5	5	5	5	5	5	5	5	5	4
Biopsy	4	5	5	4	5	5	4	5	4	5
Chemotherapy	5	5	5	5	5	5	5	5	6	5
ECG	4	4	4	4	4	4	4	4	4	4
Ultrasonography Breast	4	4	4	4	4	4	4	4	4	4
CRX	4	4	4	4	4	4	4	4	4	4
NP2	4	4	4	4	4	4	4	4	4	4
Internist	4	5	4	5	5	4	5	5	5	5
ConsultOC	4	4	5	5	4	5	5	5	5	5
SNP	2	2	2	2	2	2	2	2	2	2
POS	2	2	2	2	2	2	2	2	2	2
SNI	2	2	2	2	2	2	2	2	2	2
Service level	**[85%, 90%]**	**[90%, 94%]**	**[90%, 94%]**	**[90%, 94%]**	**[90%, 95%]**	**[90%, 94%]**	**[90%, 94%]**	**[91%, 95%]**	**[90%, 93%]**	**[90%, 95%]**

Table 14: Experimental results for biweekly schedules (Base Scenario)

Base Scenario												
Experiment (#)	BA.1		BA.2		BA.3		BA.4		BA.5		BA.6	
NP1	6	[54%, 55%]	6	[54%, 55%]	6	[54%, 55%]	6	[54%, 55%]	6	[54%, 55%]	6	[54%, 55%]
MRI	3/4	[80%, 83%]	3/4	[80%, 83%]	4	[70%, 72%]	5	[56%, 57%]	5	[56%, 57%]	5	[56%, 57%]
PET	3/4	[80%, 83%]	3/4	[80%, 83%]	4	[69%, 71%]	3/4	[80%, 83%]	3/4	[80%, 83%]	3/4	[80%, 83%]
EF	4	[78%, 80%]	4	[78%, 80%]	5	[62%, 64%]	4	[78%, 80%]	4	[78%, 80%]	5	[62%, 64%]
Biopsy	5	[45%, 47%]	5	[45%, 47%]	5	[45%, 47%]	5	[45%, 47%]	5	[45%, 47%]	5	[45%, 47%]
Chemotherapy	6	[51%, 53%]	6	[51%, 53%]	6	[51%, 53%]	6	[51%, 53%]	6	[51%, 53%]	6	[51%, 53%]
ECG	4	[70%, 72%]	3/4	[81%, 84%]	3/4	[81%, 84%]	3/4	[81%, 84%]	4	[70%, 72%]	4	[81%, 84%]
Ultrasonography Breast	4	[67%, 70%]	3/4	[78%, 80%]	3/4	[78%, 80%]	3/4	[78%, 80%]	4	[67%, 70%]	4	[78%, 80%]
CRX	4	[68%, 70%]	3/4	[78%, 81%]	3/4	[78%, 81%]	3/4	[78%, 81%]	4	[68%, 70%]	4	[78%, 81%]
NP2	4	[69%, 72%]	3/4	[80%, 83%]	3/4	[80%, 83%]	3/4	[80%, 83%]	4	[69%, 72%]	4	[80%, 83%]
Internist	3/4	[84%, 87%]	3/4	[84%, 87%]	5	[59%, 60%]	5	[59%, 60%]	5	[59%, 60%]	5	[59%, 60%]
Consult OC	5	[58%, 60%]	3/4	[83%, 86%]	5	[58%, 60%]	5	[58%, 60%]	5	[58%, 60%]	5	[58%, 60%]
SNP	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]
POS	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]
SNI	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]	2	[29%, 31%]
Service level	[67%, 77%]		[61%, 72%]		[82%, 89%]		[81%, 89%]		[89%, 94%]		[90%, 95%]	
Average utilisation	68%		74%		66%		68%		64%		63%	
Average throughput time (in days)	[13.5, 15.4]		[14.3, 16.4]		[11.8, 12.9]		[11.9, 13.0]		[11.2, 12.0]		[11.1, 11.9]	

Table 15: Experimental results (Scenario 1)

Experiment	Queuing model	j	k	l
NP1	5	6	5	5
MRI	4	4	5	4
PET	4	4	4	4
EF	5	5	5	5
Biopsy	4	5	5	5
Chemotherapy	5	5	5	6
ECG	5	4	4	4
Ultrasonography Breast	4	4	4	4
CRX	4	4	4	4
NP2	4	4	4	4
Internist	5	5	5	5
ConsultOC	5	5	5	5
SNP	2	2	2	2
POS	2	2	2	2
SNI	2	2	2	2
Service level	[85%, 89%]	[90%, 94%]	[90%, 93%]	[90%, 93%]

Table 16: Experimental results (Scenario 2)

Experiment	Queuing model	m	n	o	p
NP1	5	6	6	6	6
MRI	5	5	5	5	5
PET	5	5	5	5	4
EF	5	5	5	5	5
Biopsy	4	5	5	5	5
Chemotherapy	5	5	5	5	6
ECG	5	5	5	5	4
Ultrasonography Breast	5	4	4	5	4
CRX	5	4	5	4	4
NP2	5	5	4	4	4
Internist	5	5	5	5	5
ConsultOC	5	5	5	5	5
SNP	2	2	2	2	2
POS	2	2	2	2	2
SNI	2	2	2	2	2
Service level	[86%, 89%]	[91%, 94%]	[90%, 94%]	[90%, 94%]	[90%, 94]

Table 17: Experimental results (Scenario 3)

Experiment	Queuing model	q
NP1	5	6
MRI	5	5
PET	5	5
EF	5	5
Biopsy	4	5
Chemotherapy	5	6
ECG	5	5
Ultrasonography Breast	5	5
CRX	5	5
NP2	5	5
Internist	5	5
ConsultOC	5	5
SNP	2	2
POS	2	2
SNI	2	2
Service level	[76%, 81%]	[92%, 95%]

Table 18: Experimental results (Scenario 4)

Experiment	Queuing model	r	s
NP1	7	7	7
MRI	6	6	6
PET	6	6	6
EF	6	6	6
Biopsy	5	6	6
Chemotherapy	6	7	7
ECG	6	6	6
Ultrasonography Breast	6	5	6
CRX	6	6	5
NP2	6	6	6
Internist	6	7	7
ConsultOC	6	7	7
SNP	2	2	2
POS	2	2	2
SNI	2	2	2
Service level	[80%, 85%]	[91%, 93%]	[90%, 93%]

Table 19: Experimental results (Scenario 5)

Experiment	Queuing model	t	u
NP1	4	5	5
MRI	4	4	4
PET	4	4	4
EF	4	4	4
Biopsy	3	4	4
Chemotherapy	4	4	4
ECG	4	4	4
Ultrasonography Breast	4	3	4
CRX	4	4	3
NP2	4	4	4
Internist	4	4	4
ConsultOC	4	4	4
SNP	2	2	2
POS	2	2	2
SNI	2	2	2
Service level	[83%, 86%]	[90%, 94%]	[90%, 94%]

Table 20: Requested consults OC and treatments with their corresponding time

		Base Scenario		Scenario 1		Scenario 2		Scenario 3		Scenario 4		Scenario 5	
	Duration (in minutes)	**# treat-ments**	**min utes**	**# treat-ments**	**min utes**	**# treat-ments**	**min utes**	**# treat-ments**	**min utes**	**# treat-ments**	**min utes**	**# treat-ments**	**min utes**
Consult OC	60	2.9	176	3.1	188	3.2	192	3.5	212	4.4	264	2.4	142
Total (in hours/week)	**-**		**3**		**3**		**3**		**4**		**4**		**2**
First AC	120	2.4	286	2.5	305	2.6	313	2.9	344	3.6	428	1.9	230
Other AC	120	9.6	1149	10.3	1231	10.5	1255	11.5	1382	14.4	1724	7.7	925
First PTC	390	0.7	289	0.8	309	0.8	317	0.9	351	1.1	438	0.6	235
Other PTC	240	11.5	2764	12.2	2934	12.6	3020	13.9	3344	17.4	4170	9.3	2232
FEC	180	0.3	53	0.3	59	0.3	58	0.4	64	0.5	86	0.3	46
TAXOL	135	4.3	578	4.5	603	4.8	643	5.2	696	6.5	875	3.5	479
Total (in minutes/week)	-	28.8	5120	30.6	5441	31.5	5605	34.7	6181	43.4	7721	23.3	4147
Total (in hours/week)	-		85		91		93		103		129		69
Total (in beds/week)	**-**		**1.9**		**2.0**		**2.1**		**2.3**		**2.9**		**1.5**