

Improving care of children with cancer in Egypt



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The Sahlgrenska Academy

2014

ISBN 978-91-628-8730-8
Printed by Ineko AB, Gothenburg

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Gothenburg 2014

Front cover illustration: “*At the hospital with Mom and Dad*” Mariam Hassan

Improving Care of Children with Cancer in Egypt.

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ISBN 978-91-628-8730-8

<http://hdl.handle.net/2077/34400>

Printed in Gothenburg, Sweden

Ineko AB

To Mostafa, Mariam, Lina and Hassan-

-You are the light in my life-

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ABSTRACT

Aims: More than 70 percent of the children diagnosed with cancer in Egypt die every year. In Sweden the corresponding figure is close to 20 percent. The aims of this study was to investigate psycho-oncological predictors of mortality, parental perception of the care their child received as well as of the health care professionals, in order to improve care of children with cancer. The main hypothesis was that parental degree of trust affects a child's adherence to treatment, dose intensity and therefore survival.

Methods: During an 18-month preparatory phase, we carried out in-depth interviews, participant observations at the hospital, construction of two study-specific questionnaires, face-to-face validation of the questionnaires, and thereafter, a pilot study testing the logistics. Following that, the main data collection was carried out during the recruitment period of February to September in 2008. The eligible study population was parents of children newly diagnosed with a malignancy and admitted to receive a first chemotherapy cycle at the Children's Cancer Hospital in Cairo, Egypt. The parents were approached twice, first prior to their child's first chemotherapy cycle and then again before the third. Among the 313 eligible parents, 304 (97%) answered the first questionnaire, and 281 (92%) the second one.

Results: We found that parents reported a higher degree of trust in the medical care provided (RR 32.0; 95% CI 15.2-67.7) when they were met with care by their child's physician. Having received information concerning the disease (RR 13.2; 95% CI 7.8-22.3) and treatment (RR 17.2; 95% CI 9.5-31.4) resulted in higher trust in the health care and the physicians. Also, we found that 72 percent ($n=219/304$) of the parents had their child's disease disclosed by the physician. Among those, 39 percent ($n=85/219$) of the children were present during the conversation. Less than half of those children (45%) were below the age of 5. Also, 68 percent ($n=123/181$) of the parents reported that their child did not take the prescribed medication while at home and the two main predictors reported by the parents were child's resistance (90%, $n=111/123$) and inadequate information provided (81%, $n=100/123$). Finally, five years after the study was conducted, we observed a survival rate of 58 percent ($n=176/304$) with a 10 percent lost to follow-up. Among the studied children, we could, however, not relate the mortality to any of the psychosocial predictors addressed in this thesis.

Conclusion: Our main hypothesis that the degree of parental trust in the health care system and physicians affects the child's adherence to treatment, dose intensity, and thereby the survival rate, was not confirmed. We found an association between information provision and how it is provided with trust and adherence, yet none of these predictors were associated with the obtained survival rates. The observed survival rate of the children in our group is 58 percent, with an addition of 10 percent lost to follow-up. This is an increase as compared to official statistics of earlier years. Adherence to medication while at home was associated with parental degree of trust in physicians and health care professionals, but not with survival rate. We found an association between whether before the child's first chemotherapy cycle 1) information to parents was provided or not, and 2) how it was provided, with the degree of trust reported by the parents before the child's third chemotherapy cycle.

Keywords: Childhood cancers, psychosocial oncology, cancer care in Egypt

ISBN: 978-91-628-8730-8

LIST OF PAPERS

This thesis is based on the following articles, referred to in the text by Roman numerals:

- I. **El Malla H**, Kreicbergs U, Steineck G, Wilderäng U, El Sayed Elborai Y, Ylitalo N. Parental trust in health care – a prospective study from the Children’s Cancer Hospital in Egypt. *Psychooncology*. 2013;22:548-54.
- II. **El Malla H**, Kreicbergs U, Ylitalo Helm N, Wilderäng U, El Sayed Elborai Y, Elshami M, Steineck G. Cancer disclosure – account from a pediatric oncology ward in Egypt. *Submitted*.
- III. **El Malla H**, Ylitalo Helm N, Wilderäng U, El Sayed Elborai Y, Steineck G, Kreicbergs U. Adherence to medication: a nation-wide study from the Children’s Cancer Hospital, Egypt. *World Journal of Psychiatry*. 2013; 3:25-33.
- IV. **El Malla H**, Kreicbergs U, Steineck G, Aboulnaga S, Elshami M, El Sayed Elborai Y, Wilderäng U, Ylitalo Helm N. Advances in pediatric oncology – a five-year nation-wide survival follow-up at Children’s Cancer Hospital in Egypt. *Submitted*.

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1 INTRODUCTION

As a senior psychology student at the American University in Cairo (AUC) in 2000, I was asked to join a research group at the university in collaboration with the National Cancer Institute in Cairo, Egypt. The assigned research was aimed at mapping, comprehending and illustrating the psycho-oncological side of the children sick with cancer in Egypt, their families, and the health care situation in general and the treating physicians specifically. This was the toughest job I had ever undertaken, yet it turned out to be the most scientifically and humanitarian fulfilling task I had pursued up to that time. During these years, I came across these questions: “Why are those children suffering so much?” “Why is the mortality rate in Egypt so high compared to Sweden and the US?” Many different answers were provided ranging from “they don’t have equal treatment” or “they are not as advanced in medicine as we are in Sweden” and many more answers would be provided, none of which ever satisfied my quest.

During those years, I observed a major obstacle in the communication between the children, the health care professionals and the families. Information sharing was barely visible, and I saw that well-established relationships between patients and physicians simply did not exist. Thus, the confidence that can be created by such relationships, relationships I perhaps had assumed would be present, was absent.

For me, this was a strong motivation to go on and pursue additional research. I was constantly preoccupied by the fact that so many children are dying every year in the cancer hospitals and many more at home that we do not even know of. I thought that perhaps the low survival rates were not entirely due to lack of appropriate treatment, and that perhaps the child’s psychosocial (psychological and social) environment, as shaped by the parents, the extended family, the health care system and the physicians, would have an impact.

At that time, and unfortunately even today, barely any data exists about this group. So, in 2005, I decided to conduct a study for my master’s thesis in Egypt and find out about children’s and parents’ as well as physicians’ experiences of cancer, the social and emotional consequences of having one’s child diagnosed with cancer and how it reflects on the child, the family and the health care system. The thesis title was “*A study of how Egyptian children with cancer, their parents and physicians perceive the illness and hospital stay from a health psychology perspective*”. I had no literature to build on from; therefore, I had to start from scratch and use the data I had collected in the preceding years beginning in 2000 and ending in 2003. From the material I had collected during those three years, I observed several psychosocial issues that appear to interfere

with the parents' well-being, which apparently seemed to influence the child's physical and emotional health.

Cancer care today often provides up-to-date biomedical treatment but fails to address the psychosocial problems associated with the disease. This failure can compromise the effectiveness of health care and thereby adversely affect the health of the cancer patient. Psychological and social problems created or exacerbated by cancer include emotional problems, lack of information or skills needed to manage the disease, time-consuming, long, expensive and exhausting transportation, lack of other resources, and disruption in work, school and family life. All of these factors cause additional suffering, weaken adherence to prescribed treatments, and threaten the patient's return to health. This was the driving force behind my decision to do the research for this thesis since we hypothesized that parents who do not have a proper parent-physician relationship and receive adequate, comprehensible and concrete information about their child's disease and treatment will not trust health care providers as much as the parents who do experience an excellent parent-physician relationship. These parents will more likely be late to the treatment appointment or may not show up at all as they have not been informed about the significance and consequence of not following the chemotherapy regimen on a fixed schedule. The more I thought about all of these factors, the more I wondered if those unmet psychosocial needs might turn out to be factors associated with the low survival rates. Being left with these questions, I decided to seek an education in science to find out if and what psychosocial features may partially account for the low survival rates that were found at that time in Egypt.

The pre-study that this thesis is based on is extracted from my 10 years of experience in pediatric oncology wards in Egypt and mainly my master's thesis work at Linköping University in 2005, which entailed the data collection conducted in Egypt at Cairo's three major governmental oncology wards. The main study, however, was made in 2008 at the state-of-the-art, non-governmental, and only child oncology hospital in Egypt and the largest in Africa; namely the Children's Cancer Hospital in Cairo (CCHE), which was founded in 2007.

Throughout the research leading to this thesis, during the construction of the questionnaires and throughout the analysis and writing-up phase, I had interactions with many specialists who became involved. I was fortunate in having available a pediatrician, a specialist nurse in childhood cancer, and a professor in oncology and epidemiology, all from different institutions in Sweden, and all able to contribute their special knowledge. I was also fortunate in being able to interact with a pediatric oncologist, a psychiatrist and a psychosocial specialist, as well as a professor in oncology from the hospital in Egypt. The whole team was a tremendous resource throughout the thesis work.

The journey has been long, progress has been achieved to some extent and the survival rates luckily seem to be increasing. Yet much more remains to be accomplished. Personally, this thesis is a start of a long journey into the fascinating realm of knowledge and learning as well as being keen and passionate about every child and parent I come across. My passion for those children will always be the source of the compelling energy to pursue this journey of mine.

*Hanan El Malla
November 10, 2013
Gothenburg, Sweden*

2 BACKGROUND

2.1 PEDIATRIC MALIGNANCIES

Cancer is a generic term for a large group of diseases that can affect any part of the body. Other terms used are malignant tumors and neoplasms. Childhood cancer is not a single disease; there are many different types. Compared with adult cancers, childhood cancers tend to have different histologies and occur in different sites of the body. One defining feature of cancer is the creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs. This process is referred to as metastasizing. Metastases are the major cause of death from cancer [1].

Leukemia is the most common type of childhood cancer, representing about one third of all cancers in children less than 15 years of age. Leukemia is a condition where too many underdeveloped white blood cells are found in the blood and bone marrow. Four fifths of childhood leukemias are acute lymphatic leukemias (ALL); other types include acute myeloid leukemia (AML) and chronic myeloid leukemia (CML). Brain tumors are the most common solid tumors in childhood, and make up about a fifth of all children's cancers. There are many different types of brain tumors: medulloblastoma, astrocytoma and brainstem glioma are the most common. Neuroblastoma (sympathetic nervous system), retinoblastoma (eye), Wilms tumor (kidneys), and hepatoblastoma (liver) are most usually found in infants or young children. Other malignancies found in children and young adults include lymphomas (Hodgkin and non-Hodgkin lymphoma), soft tissue sarcomas (including rhabdomyosarcoma), bone cancer (osteosarcoma and Ewing sarcoma), plus a number of other less common childhood cancers. Histiocytosis is rare; it is not thought to be a true cancer, but in many respects it behaves like one [1].

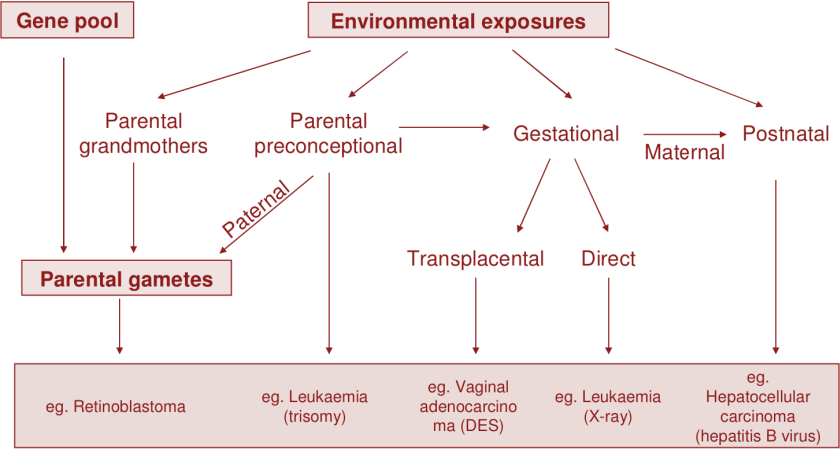
Unlike normal cells, cancer cells do not stop reproducing after they have doubled 50 or 60 times. This means that a cancer cell will go on and on and on doubling. Furthermore, cancer cells do not obey signals from other cells. Something in the cancer cells overrides the normal signaling system. This may be because the genes that tell the cell to reproduce keep on sending signals. Or it may be because the genes that normally tell the cell to stop reproducing have been damaged or lost. So the cancer cell keeps on doubling, regardless of the damage the extra cells cause to the part of the body where the cancer is growing [1].

Cancer cells do not stick together; they can lose the molecules on their surface that keep normal cells in the right place. So they can become detached from their neighbors. This partly explains how cancer cells spread to other parts of the body [1].

2.1.1 ETIOLOGY AND OCCURENCE

Cancers occur when genetic and environmental factors interact in a multistage sequence [2] (Figure 1). In a small percentage (5-15%) of childhood cancers, familial or genetic factors are thought to predispose the child to cancer [3,4]. An even smaller percentage (<5-10%) of childhood cancer has an identified environmental link [3,4]. Although some studies have concluded that genetic factors make a minor contribution to most types of cancer [4], the majority (75-90%) of childhood cancers, however, remain poorly understood and causes are unknown [3,4]. There is no doubt that it is a combination of factors acting concurrently and sequentially that are involved with any individual case of childhood cancer.

Figure 1. Schematic framework for considering cancer etiology (Based on Anderson LM)



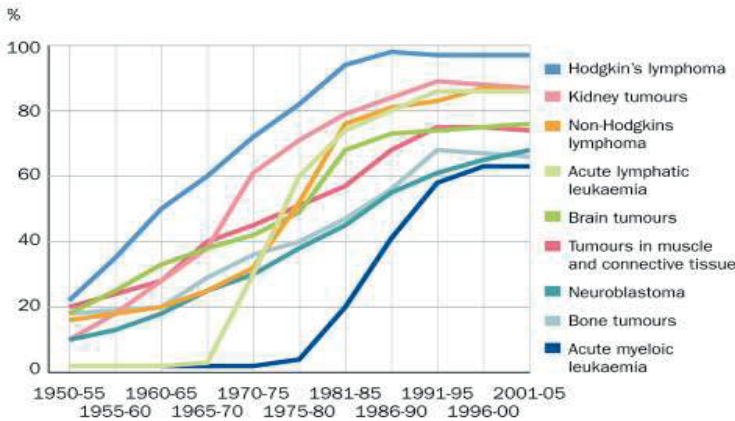
Although specific types of childhood cancer are uncommon and childhood cancers represent a small percentage of all cancers, each year more than 175 300 children are diagnosed with the disease in the world [5]. Of this total, the great majority of children, and 80 percent of children with cancer, live in developing countries, and contribute significantly to the estimated 96 400 childhood cancer

deaths annually; thus collectively childhood cancers represent an important global public health problem [5].

In Sweden, approximately 300 children are diagnosed with cancer every year [6]. This figure has not changed since the 1950s. At that time, a child cured from cancer was rare; currently three out of four children suffering from cancer become long-term survivors. Over the last decade, the greatest success has been achieved in the treatment of acute lymphatic leukemia (ALL), lymphomas, and renal tumors; more than 80 percent of children are now cured. Until 1970, only five percent of children suffering from ALL survived [6].

Leukemia and brain tumors are some of the most common cancers in children in Sweden. Figure 2 shows the survival rates in percentage from different cancer diagnoses in children in Sweden. In all cases, survival rates have improved considerably from the 1950s to the present day [6].

Figure 2. Survival rates in percentage from different cancer diagnoses in children from 1950 to 2005 (Swedish Childhood Cancer Foundation)



In the United States in 2012, approximately 12 060 children under age 15 were expected to be diagnosed with cancer and about 1340 children are expected to die from the disease (Table 1). Although this makes cancer the leading cause of death by disease among US children 1 to 14 years of age, cancer is still relatively rare in this age group. On average, 1 to 2 children develop the disease each year for every 10 000 children in the United States [1]. Mortality rates for childhood cancer have declined by 66 percent over the past four decades, from 6.5 (per 100 000) in 1969 to 2.2 in 2008. The substantial progress in reducing childhood cancer mortality is mainly due to improvements in treatment [5].

Table 1. Cancer incidence and mortality in children age 0-14

Country	Total Population (millions)	Population <14 years n (%) (millions)	Cancer Incidence n	Cancer Mortality n (%)
<i>Worldwide</i>	7 022	1 829 (26)	175 300	96 400 (55)
<i>Egypt</i>	83.7	26.8 (33)	8 500*	5 950 (70)**
<i>Sweden</i>	9.1	1.4 (15)	300	75 (25)
<i>USA</i>	313.8	62.9 (20)	12 060	1 340 (11)

* An overall estimate by the Children's Cancer Hospital, Egypt in 2008

** An estimate according to WHO in 2001

In Egypt, a large uncertainty accompanies statistics for cancer incidence and survival. Of the 18 496 new cancer cases with confirmed and registered malignancy at the National Cancer Institute in Egypt between January 2002 and December 2003, 1 937 (10.5%) were children under the age of 20 years [7]. As many as 1 184 (61%) were boys and 753 (39%) were girls, with a boy-girl ratio of nearly 1.57 [7]. According to Children's Cancer Hospital, 8 500 children are estimated to be diagnosed with cancer in Egypt every year [8]. The new Children's Cancer Hospital had 1 862 admitted cases during 2008, which approximately account for one-fourth of all children diagnosed with cancer in Egypt 2008 [8]. It is difficult to measure the incidence of childhood cancer accurately in developing countries, where cases are often unreported due to greater frequency of deaths from infectious diseases and malnutrition [5]. The great majority of children, and 80 percent of children with cancer live in developing countries [9] and more than 60 percent of the world's children diagnosed with cancer have little or no access to effective therapy [5]. Moreover, more than 70 percent of all children diagnosed with a malignancy in the developing countries die every year [10]. The geographic and socioeconomic inequalities in cancer treatment pose challenges that have only began to be addressed [11].

There are fifteen specialized pediatric cancer wards spread throughout Egypt, but the major ones are in the capital, Cairo. In 2007, the largest pediatric oncology hospital in North Africa and the Middle East opened in Cairo, the Children's Cancer Hospital (CCHE). CCHE is a non-governmental hospital, offering free of charge health care service to the entire country. The hospital currently houses 187 inpatient beds, a 300-500 patient capacity outpatient department, a specialized clinical pharmacy, intensive care and bone marrow

transplant units, a comprehensive surgery department and multi-specialty clinics. CCHE is the only pediatric cancer hospital in Egypt.

2.1.2 CHEMOTHERAPY, DOSE AND DOSE INTENSITY

In general, cancer treatment varies from surgical removal of the tumor/tissues around it, powerful doses of chemotherapy and/or extensive exposure to radiation. Chemotherapy entails the administration of strong drugs that target fast-growing cells, medicines that also affect other functions of the body causing hair loss, indigestion and other side effects. Radiation treatment, on the other hand, use radiation to destroy malignant cells, yet, healthy tissues are also damaged. Surgery used to remove the tumor may lead to permanent recovery, but undetected malignant cells may already have metastasized to other organs or moved from their original location in connection with the surgery. Therefore, each treatment type results in a certain level of risk and pain to the child, but if the cancer cells are left untreated they will ultimately damage vital organs and/or the whole circulation of the body so absence of treatment is not seen as an option [12].

Cytotoxic chemotherapy involves scheduling a series of treatment sessions at which a “cycle” is administered. The time interval between each “cycle” session is specific for each patient (e.g. one week, two weeks, three weeks). Each treatment “cycle” entails a certain dose, which is based on a calculation of the child’s weight and height. A treatment “cycle” is provided during a certain period of time, e.g. hours, or days at the hospital where the child is admitted to the in-patient unit. Usually, the child is discharged when the treatment “cycle” is completed, to be back for the next “cycle” within a planned period of time, a week, two weeks, three weeks or more, depending on the specific treatment protocol provided to the individual child. Correct dose-intensity is received when each “cycle” is administered within the planned time-span. When delays occur, it is no longer possible to reach the planned dose-intensity, which may result in further complications such as metastases or even mortality [12].

2.2 PEDIATRIC CANCER IN EGYPT

Childhood cancer in Egypt is a growing concern for the society since its incidence has been increasing rapidly. The high mortality rate is assumed, in the literature, to be due to the inadequate access to medical care in developing countries as there are very few hospitals or centres existing in these countries with CCHE being an exception to the rule. Lack of education and knowledge of health concerns particularly relating to children have delayed many families from seeking medical help and treatment [10]. In addition, lack of transportation for the patients or obstacles concerning transportation from rural to urban places makes the available health care inaccessible [10]. Moreover, limited

accessibility to antibiotics and chemotherapeutic drugs makes the treatment ineffective as the treatment in this case is based on availability and not efficacy [10].

According to the most current published statistics in Egypt, pediatric cancer incidence in Egypt is occurring in $n=862$ (9.4%) of the young population below 20 years of age [13]. The etiology of cancer is known to be quite vague and unspecific, however, there are some theories suggesting that cancer, partly and in general, in the Arab World can be due to the factors shown in Table 2 [13]:

Table 2. Etiology of cancer in Egypt (NCI, Egypt)

- Increase in smoking prevalence
- Increase of incidence of hepatitis B and C
- “Westernization” of social and dietary habits
- Lack of physical activity
- Low socio-economic status
- Population average age increase
- Reduction in the incidence of infectious diseases

In Egypt the mean age of cancer patients is 48 years, which is two decades younger than the mean age of American cancer patients [13]. This is a reflection of the young age structure of the Egyptian population, with 33 percent below the age of 15 [9] and 50 percent below the age of 20 years [13].

Usually the child is discharged from the hospital when the chemotherapy cycle is completed. If the child does not return to the next planned appointment, the hospital’s possibility of contacting the family is limited. Thus, to avoid having the child’s next treatment cycle delayed, resulting in a decrease in delivered dose-intensity, the family has to be informed of the consequences of a delay, which requires proper communication between the health care professionals and the family. The level of confidence is challenged when nausea, infections and other treatment-related complications occur in the child’s home between cycles.

Nonetheless, CCHE is assumed to have increased the survival rates of pediatric cancer in Egypt. CCHE has resources that were not previously to be found in Egypt such as highly advanced up-to-date treatment protocol and a holistic cancer treatment offering radiation and surgery and physiotherapy departments, and is free of charge and available to everyone. The hospital has an electronic journal system and offers high technology up-to-date equipment and treatment protocols that correspond to the protocols in the US with modifications tailored

for the children in Egypt. Aside from that, the hospital houses a specialized clinical pharmacy, intensive care and bone marrow transplant units, a comprehensive surgery department and multi-specialty clinics, including a wide range of specialists, for example: orthopedics, cardiology, psychiatry, ophthalmology, otorhinolaryngology (ear-nose-throat), and neurology. According to the latest official 5-year survival rate from CCHE that was published in 2012 (Table 3), the survival rates have increased dramatically and some have reached the rate in Sweden and the US. Nevertheless, CCHE only accommodates one-fourth of all children in Egypt diagnosed with cancer.

Table 3. Five-year overall survival rate from the Children’s Cancer Hospital, Egypt, in 2012

Diagnoses/type	Survival rates
Leukemia	
ALL	80%
AML	65%
Lymphomas	
Non-Hodgkin	80%
Hodgkin	95%
Brain	66%
Osteosarcoma	77%
Sarcomas	70%

2.3 LIVING WITH A MALIGNANCY

Pediatric cancer has been characterized to result in suffering, pain, social alienation, and, in some instances, even disfigurement [14]. The pain of the treatment, the fear of having physical changes such as hair loss, weight gain, and infertility affect the child’s body, mind and social relationships and the parents’ as well. In addition, treatment of all forms of cancer, including pediatric cancer, entails the expenditure of a great deal of money, time and effort, as patients go through painful treatments, several hospitalizations, changes in physical appearance, financial pressures (though the treatment is free of charge, the parents are forced to take unpaid leave from work) and even changes in their relationships with their parents, siblings and peers.

Cancer is stigmatized in Egypt, where there are many misconceptions associated with having cancer. Most people think that cancer is a death penalty. In addition, when a young child is diagnosed with cancer, in most cases, the surrounding society may take a side, not allowing the neighboring children or cousins to play with the child or to visit the family so as not to be “infected” with the disease. Other forms of stigmatization may be a “bad” reputation of not being able to

marry in the future due to the assumed infertility that many believe the treatment will bring about or due to assumption that cancer runs in generations and there is thus a risk associated with marrying into the family of a sick child. Unfortunately, there is no published literature in international journals on this part of the world that address the stigma of childhood cancer. Thus, I can only address my experiences from the hospitals where I have conducted several studies.

2.4 PSYCHOSOCIAL NEEDS OF CHILDREN WITH MALIGNANCIES

The diagnosis of a child with cancer is extremely disruptive to the family and creates a crisis even in the most balanced family. The diagnosis and treatment changes the daily life of the child and other family members and have an impact on their physical and psychological well-being. It also lowers the child's self esteem, distances the child from peer groups and therefore requires help, in many cases, of a psychologist.

The term “psychosocial health” refers to being mentally, emotionally, socially, and spiritually well (Figure 3) [15]. Attending to the psychosocial needs of patients should be an integral part of quality cancer care [16]. Meeting the psychosocial health needs of a patient is usually referred to as providing psychosocial health services, defined as “psychological and social services and interventions that enable patients, their families, and health care providers to optimize biomedical health care and to manage the psychological/behavioral and social aspects of illness and its consequences so as to promote better health” [16].

Figure 3. Defining “psychosocial health” (Donatelle RJ et al.)



The European Society of Paediatric Oncology (SIOPE) has set standards in 2009 for pediatric psychosocial care [17]. The standards state that psychosocial support is an integral part of treating children and teenagers with cancer and of their families; also, psychosocial care requires the team to help the patients and their families through all procedures, treatment and palliative care where necessary, helping them to cope with the stress involved, pre-empting the potential for crisis and attempting to maintain a good quality of life throughout [17]. Furthermore, each child or young person with cancer and his or her family should be offered psychological help by a psychologist, social worker and teacher/play therapist [17]. The quality of life of the child and the family can be greatly improved by social, psychological and educational care, communication of information about the disease, its treatment and impact on the family, information provided to children that is appropriate to their level of understanding, maintenance for the child to remain active and continue life as normal as possible, helping the child to reintegrate into school and society in general, once treatment is completed [17]. Besides information provision about disease, treatments, help in coping with emotions accompanying disease and treatment, help in managing the disease and assistance in changing behaviors to minimize impact of disease; psychosocial needs can also be in the form of material and logistic resources such as transportation, help in managing disruption in school and family life and financial advice and/or assistance [16].

Many people living with cancer report that their psychological health care needs are not well addressed in their care. Throughout diagnosis, treatment, and post-treatment, patients report dissatisfaction with the amount and type of information they are given about their diagnosis, their prognosis, available treatments, and ways to manage their disease and health [16]. Health care providers often fail to communicate this information effectively, in ways that are understandable for the parents and that can enable action by parents [18]. Moreover, individuals diagnosed with cancer often report that their providers do not understand their psychosocial needs, and they do not consider psychosocial support as an integral part of their care [16].

Most studies on children and cancer in Egypt have been made from a medical perspective. Research conducted from psychological and social perspectives deals mainly with sick children from a Western point of view. Studies on children with cancer from social, cultural and psychological perspectives are rare in the Arab World.

2.5 PATIENT–PHYSICIAN RELATIONSHIP

The fundamental interaction in health care is the one between patient and physician. The patient–physician relationship is the very heart of health care delivery, and is the benchmark to which the health care system must align. It

pervades each component discussed in this thesis. In the context of this thesis, I am addressing the patient–physician relationship as a synonym to the parent–physician relationship.

The patient–physician relationship is essential to providing and receiving excellent care, to the healing process and to improved outcomes. At its best, the patient–physician relationship not only provides access to health care but also can promote healing as evidence demonstrates the direct effectiveness of its relation to health outcomes [19]. It is therefore important to understand and identify the components of this relationship. The emotions and the private, very often uncomfortable sharing of information between patient and physician require a foundation of mutual responsibilities that include respect, open and honest communication, trust and a mutual desire to improve health outcomes [19]. The patient–physician relationship may be a therapeutic relationship and often includes family members, friends and other health care professionals.

Cancer treatment involves a relationship between the child, his or her family members and the treating physicians and the entire health care professionals. The World Health Organization proposed that cancer treatment should involve a long-term physician–patient relationship due to the long process of diagnosis and treatment [20]. As patient–physician communication and patient satisfaction are important elements of cancer care [21,22,23], establishing and maintaining a good relationship between the caregivers and the parents of a child diagnosed with cancer may bring a wide range of positive outcomes to the parents and their child. For instance, a high level of satisfaction with the child’s physician can play a vital role in improving the child’s health-related quality of life [24]. The role of trust in the medical setting has been acknowledged for many years [25] and is generally considered to be a central part of the patient–physician relationship [26]. Furthermore, the communication between the health care providers and the patient is an important factor affecting the degree of adherence [27], when patients understand their physicians they tend to follow their treatment regimen and modify their behavior [28]. Adherence is an important element in treating patients within the patient–physician relationship, especially those with life-threatening diseases such as cancer. Additionally, in a study made by Safran et al., trust was found to be a key element in the patient–physician relationship and older patients who trust their physician were among those who complied best with the medical regimen [29]. Also, if the child and parents understand their physician, they are more likely to follow the physician’s recommendations and the suggested treatment schedule [30], which in turn will increase the likelihood of being cured. Providing adequate information regarding both treatment and prognosis and having this information delivered in a proper manner are actions that may increase trust among parents of cancer sick children [31].

2.5.1 COMMUNICATION APPROACH

The importance of communication in creating a good patient–physician relationship has been reflected in research in a Western context. There are several factors, however, that may have an influence on the communication between physicians and patients. For example, Ben-Sira proposed that the severity of the disease interacted with the physician’s communication style to determine the patient’s satisfaction [32,33]. Communication may also be of importance in the actual curing process [34].

There are several communication styles that increase the patient’s satisfaction and as a result increase the level of the patient’s adherence. Affective communication is one of the communication styles that has been shown to increase the patient’s satisfaction [35]. Proponents of affective communication mainly encourage physicians to handle the patient with affect, to treat them as human beings and not just as one of the cases they encounter everyday [35]. This style also encourages physicians to give enough time to their patients, to show interest in them, and to explain to them what is going on [36]. Affiliation is also another communication style that is favored by patients. Affiliation signifies that physicians show interest, warmth, empathy, and friendliness and are genuine with their patients [36]. In one study, patients were most satisfied when physicians used affiliation and affective communication while decreasing their exercise of power [36].

Another important aspect of the communication that increased the satisfaction of the patients was the use of positive words. Hall et al., state that it is very important that physicians become more reassuring and use positive words, while sustaining a normal tone [25]. Positive words with a negative tone were more favored than negative words with a positive tone [25]. However, it will be more essential for the patient that the physician can be warm and show concern (for the patient) for their situation when they are providing the patient with the information [25]. This behavior would imply that the physician actually cares for his or her patient, as the physicians will include a socio-emotional aspect to care as opposed to caring only about the physical body [25].

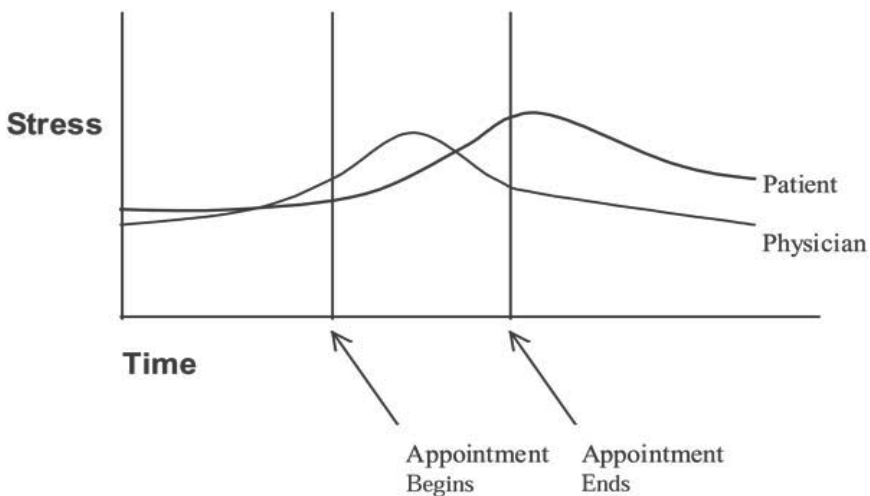
2.5.2 COMMUNICATION AS A COMPONENT OF DISCLOSURE

Communication is one of the major components of the disclosure of diagnosis [37]. Disclosure has been defined as “the act of revealing personal significant information that exposes the bearer to the risk of rejection of negative judgment” [38]. Communication in disclosure refers to how information is disclosed. Communication is also an important element within the physician–patient relationship [25]. “Medicine is an art whose magic and creative ability have long been recognized as residing in the interpersonal aspects of the patient–

physician relationship” [25]. Such an interpersonal aspect is highly dependent on the communication of the physicians. Physicians generally spend more time communicating with their patients than examining and treating them as they ask about the history of the patient, the medical complaint, and give the diagnosis and treatment options [36]. Therefore, even though the motivation of the patient to enter the clinic of the physician for the first time is mainly determined by the competence of the physician, his or her degree, experience and reputation [25]; good communication determines whether patients will continue with their physician or not [25,36].

According to Ben-Sira, most patients are very anxious when they enter the physician’s clinic for the first time, as they know very little about their condition and the prognosis [32,33]. As a result, patients become more dependent on their physicians, and hence they expect their physicians to communicate well with them to decrease their anxiety level [32,33]. On the other hand, many physicians experience distressing emotions when they deliver difficult news to a patient such as diagnosis, prognosis, treatment side effects, palliation and end-of-life issues. Ptacek and Eberhardt suggested a model of the stress related to the physician’s and patient’s experience associated with bad news [39]. This model describes the physician’s anticipatory stress before delivering bad news and suggests that the stress level for physicians peaks during the clinical encounter, whereas for the patient they peak some time afterwards [39] (Figure 4). This model suggests that communication of difficult news is not only distressing for the patient, but also for the physician and that physicians need to learn how to communicate difficult news.

Figure 4. Stress experienced by physician and patient in the discussion of bad news (from Ptacek and Eberhardt)



2.5.3 DISEASE DISCLOSURE

Disclosure of the diagnosis to patients with cancer in Egypt is a very complicated issue and has not yet been addressed in the literature. In the Western countries patient autonomy, informed consent and shared decision-making are deeply rooted in the health care system that shapes the patient–physician relationship, whereas these values are not as yet integrated in the Arab societies [40,41].

A significant percentage of cancer patients in the Arab societies are not made personally aware of their disease; physicians prefer to withhold information from the patient and disclose the cancer diagnosis to selected members of the patient’s family [40,41] or to the patient first at the time when the patient has experienced adverse effects of treatment [42].

A study from Saudi Arabia revealed that physicians express the wish to inform patients of the diagnosis but they do not know what to say or how to say it [41]. They expressed worries that breaking bad news could evoke fear and anxiety in patients and they were also concerned that the patients may not be able to cope with the difficult news [41]. In addition, one Turkish study identified the relatives of cancer patients as one of the most significant barriers to disclosure [43] and another study from Saudi Arabia revealed that relatives of cancer patients believed that disclosure of the cancer diagnosis to the patient could be harmful and bring about suffering to the patient [40]. These assumptions seem to be unrealistic as many children, in the master’s thesis conducted, had reported awareness of their disease (an awareness that was mostly withheld from the parents, physicians and health care professionals) and believed that they should be told the truth. This is addressed by studies that show that children were not deceived by the avoidance of talking about their diseases or by untrue assurance about their prognosis [44]. This is also in line with what the anthropologist Myra Bluebond-Langner addresses in her book; that children are competent social actors and may be fully aware of their disease, treatment and consequences even if adults may not inform them and they are competent enough to comprehend and participate in decisions dealing with their disease [45]. Bluebond-Langner also addresses that children’s silence is not out of ignorance but a way to hide their feelings and knowledge of dying in order to protect their parents, and abiding by what Bluebond-Langner refers to as “mutual pretense” [45]. The author means that children are responsive to this pattern of social order, and join in the pretense in order to ensure their social acceptance and worth [45].

In the master’s thesis conducted, an interesting matter observed and discussed at the treatment units is the fear of the disease itself and its name and its connotation, which in the end is really actual fear of death and stigma. Although no studies have been made of the attitudes of various groups of Egyptians

toward cancer it is worth noting some of the popular views one encounters when cancer comes up for discussion. First, cancer has always been common in Egypt among people of all ages, and it has thus been discussed and brought up mainly in movies, and the society has formed a negative idea about it as a fatal and incurable disease. This preconception has been passed on from generation to generation, as the medical system in Egypt has not yet been developed in ways that one might hope for. Also, due to the high mortality rate, the old predispositions have been strengthened, as several parents and physicians have been close to a person who has died of cancer or have heard of cancer in various ways. The fear starts by not mentioning the name of the disease as it may, for many people, be a bad omen or bring about distress or fear of becoming diseased by it. Thus, when the parents have to say the name, they usually say “the bad disease” or “the malignant disease” and straight afterwards they will say “may God protect us from it” as if saying or mentioning the disease will possibly pass it on to the person.

The decision of disclosing or withholding information from parents to a child with cancer in Egypt is not fully agreed upon by many of the physicians interviewed in my master’s thesis. Some physicians favor disclosure, some are uncertain while others do not find it essential or they do not know how to practice it. The nature of cancer and its association with death and other misconceptions make some physicians reluctant to tell the child’s parents when they are suspecting a cancer or even when they are sure of it. The severity of the disease and the stage reached dramatically changes the physician’s decision as most of them withhold such information from the parents. The dilemma of deciding the optimal methods for telling children bad news about their own cancer remains unanswered [46] and in Egypt, the decision of truth telling in general remains undisclosed and neglected due to the general preconception that it is not in the favour of the child.

2.5.4 ADHERENCE TO MEDICAL REGIMEN

Non-adherence to medical regimen is a concern in pediatric malignancies throughout the world, not least in the developing countries [47]. It is one of the major complicated issues in the pediatric oncological setting. According to the definition of the World Health Organization (WHO) in 2003, which is an update of the first definition addressed by Haynes in 1979, adherence is “...the extent to which a person’s behavior-taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider” [48]. Hence, the patient and his or her family are responsible to follow and maintain the prescribed regimen as agreed upon. In addition, the role of the health care professionals in providing clear information and explanation of the treatment options is emphasized [48]. Cessation, refrain

from or incorrect intake of cancer treatment in children can bring about serious, often life-threatening health outcomes as well as severe economic outcomes for the individual and the wider society [28,29]. It can adversely restrict the cost-effectiveness of medical care and affect the health and quality of life of the patients. Increased health care costs (extended treatment, additional physician visits, changed prescriptions), and the development of drug-resistant organisms are common outcomes of non-adherence [29,47,48]. In addition, non-adherent patients report poorer quality of life, increased suffering from disease, increased hospitalization time and increased morbidity and mortality [29,48].

Adherence can be divided into three age categories: infants, young children and teens as the characteristics of the child's life and behavior are likely to affect why they may be non-adherent to treatment [49]. As children become more autonomous, adherence tends to become more difficult to maintain. The tendency of children to run away at the time of cancer drug administration makes adherence difficult in young children [49]. Furthermore, adolescents' oppositional behavior and wanting to be like their peers may be predictors of non-adherence [49]. Despite the dangerous nature of pediatric cancers, between 10 to 50 percent of children and adolescents with cancer fail to adhere to oral medication regimes [50] and one study showed that between 27 and 63 percent of adolescent patients did not follow the prescribed oral treatment [51]. Very little is to be found in the international literature from Egypt or the Arab region regarding the importance of and the leading causal factors of non-adherence and the serious life threatening consequences as well as economical consequences of such a malpractice.

Children's suffering during their hospital stay may be reflected in their behavior when at home as children reflect their fear, apprehension and anxiety in both behavioral and physiological reactions [52]. Resistance and throwing tantrums becomes a daily pattern in the child's life, at home or in the hospital as a response to the perceived anxious situation they are in [52]. A number of studies have found several variables associated with poor adherence [48]. Adolescents and in particular males are more likely to be non-adherent [48]. Lower socio-economic status of the family in general and lower parental education level and parental separation have all been associated with non-adherence [48]. In addition, less knowledge about the disease and treatment has, in many studies, been associated with poor adherence [48]. Furthermore, diseases of longer duration, course of treatment and disease severity have been found in the literature to be associated with adherence [48]. Positive adjustments in terms of coping and higher self-esteem and parental monitoring have also been associated with adherence [48]. In a study made to determine predictors of non-adherence in chronically ill adolescents, support from nurses and physicians were found to be the most powerful predictor [50].

3 AIM

The aim of this study was to investigate psycho-oncological predictors of mortality, parental perception of the care their child receive as well as of the health care professionals they met, in order to improve care of children with cancer.

Specific aims of the research for this thesis:

1. Identifying psychosocial predictors of mortality in pediatric malignancies.
2. Investigating a five-year mortality rate in relation to psychosocial predictors.
3. Investigating the degree of adherence to prescribed medical regimen upon discharge and predictors of non-adherence.
4. Identifying the degree of information sharing about disease and treatment and its relation to parent's degree of trust in the physician, the health care professionals and the health care system.
5. Examining the rate and pattern of disease disclosure to parents and children.

4 PATIENTS AND METHODS

4.1 STUDY POPULATION

The study population for the research of this thesis comprised all parents ($n=313$) of children newly diagnosed with cancer admitted to receive a first chemotherapy cycle at Children's Cancer Hospital in Cairo, Egypt (CCHE), Egypt, during a study period of 7 months (February until September 2008).

4.2 CONSTRUCTION OF QUESTIONNAIRES

During an 18-month phase (2007-2008), we constructed the two study-specific questionnaires (*Pre-1* and *Pre-3*) according to procedures developed at the Division of Clinical Cancer Epidemiology [53,54,55] integrating qualitative and quantitative methods as described below:

1. Qualitative pre-study based on master's thesis material
2. Interviews with study population; parents of children newly diagnosed with a malignancy
3. Assignment of the content of the interviews to categories
4. Construction of questions based on the information from interviews
5. Face-to-face validation (the questions are tested on the intended population)
6. Pilot study (questionnaire administered to a small number of individuals)
7. Questionnaire administered to the entire population

4.2.1 QUALITATIVE PRE-STUDY

My master's thesis data collection was performed during 2005 and entailed formal and informal interviews with children, parents, and physicians in addition to informal interviews with the child's relatives, health care professionals present at the unit and individuals close to my informants. The data collection also entailed participant observations in the hospital setting where the patients and the parents and the health care professionals were observed and notes were taken on those observations.

In the research, I adopted a qualitative research method of data collection used in psychology; Interpretive Phenomenological Approach (IPA), common in critical health psychology. The Interpretive Phenomenological Approach method was developed to provide a closer look at the person's psychological world in relation to social and cultural context [56]. Interpretive

Phenomenological Approach is concerned with health psychology as it presupposes a bond between cognition, physical state and verbal response [57]. As my research deals with the ideas, beliefs and thoughts of the child and parent and physician at the oncology hospital, this method has been used in order to understand how these three participants view and experience life, death, the disease, the hospital stay and their world as a whole. The method does not question the individual's thoughts and ideas and view of the world as true or false, rather it aims at finding how individuals experience certain things [56]. It also acknowledges the fact that the individual's experiences, thoughts and feelings about things in life evolve from human interaction with the social surroundings [56]. The IPA method has an advantage in producing a cognitive "map" to the researcher that entails the informant's view of their situation [56]. In the master's thesis, some analytical techniques have been used from the Grounded Theory since it is very closely related to Interpretive Phenomenological Approach. Grounded Theory has broad data collection options in terms of transcription of audiotaped semi-structured interviews, participant observations, memo writing, and making use of a "focus group" [56]. The two approaches are very similar to each other as they both are concerned with "themes and categories" that arise through analysis [56] and this is what my research has been concerned with. Furthermore, they both entail "comparison" of the information and their meanings [56] which is indeed a very important theme in the process of analysis.

Three different formal interviews based on minor questionnaires were conducted and different interview guides were elaborated. A consent form was filled in for all children, parents and physicians that participated. I interviewed and observed 69 children and their parent/caregiver (in some cases I was able to see both the mother and the father and grandmothers and other relatives during the visiting hours) and 21 physicians.

The interview questions were translated into colloquial Egyptian. All formal interviews were audiotaped and transcribed in extensor to English as they are audited in Arabic. The transcriptions are not detailed in the sense that I did not include non-linguistic features. Thus, the transcriptions were the conversation; the words being said, nevertheless, I would include pauses and repetitions as I found them important to my analysis. It is vital to add that the transcriptions were not my understanding of the conversation but a direct translation into English. Moreover, some of the translations of metaphors or idioms were later translated into the context of English, which entails my own understanding of them from my experience of the country.

Furthermore, important themes were then extracted from each interview (child, parent and physician). Then, I would group the most common themes from the parent, child and physician and place them in categories, as I would refer to

them throughout my analysis. I also made several observations. The observations entailed spending hours on meetings with the physicians, children and their caregivers on a daily basis during my stay. Also, observations were made in other settings such as in the pediatric outpatient clinics, homes, and various social assemblies, attending lectures, hospitals rounds and funerals. Also, detailed accounts were made of interactions between the child and parents, physicians, nurses, relatives, visitors, strangers, and in various settings, such as the clinic waiting rooms and treatment rooms e.g for MRI, CT scan, and Radiotherapy.

4.2.2 IN-DEPTH INTERVIEWS

As a final step prior to the construction of the two questionnaires, additional interviews were conducted as open-ended and semi-structured questions. We conducted 29 in-depth interviews in 2007 at the oncology wards in three governmental hospitals in Cairo, Egypt. We followed the same analysis pattern as in the work for the master's thesis. We grouped the main concerns that the parents reported during the interviews conducted in 2005 for the master's thesis and the in-depth interviews conducted later. We set up our hypotheses and divided the questionnaires accordingly. The main categories reported by the parents were: lack of the provision of proper information, cancer disclosure concerns, and what information was provided during those critical conversations, a wish for involvement in the care of one's child, child resistance to treatment at the hospital and at home, unmet emotional needs, lack of confidence in the health care system, the health care professionals and the treatment and the fear of death of one's child.

4.2.3 CONSTRUCTION AND CHOICE OF QUESTIONS AND RESPONSE SCALES

For questions like "Overall, how would you rate the care your child receives at the hospital?" we used a response scale including the categories "very bad", "bad", "moderate", "good", and "very good". We also used attitude scales where we asked "Sometimes your child's physicians do not pay full attention to what you are trying to tell them, do you agree?" with the response scale "Do not agree at all", "Agree to some extent", "Agree to a large extent", "Agree completely". Furthermore, person-prevalence scales were used in questions like "How often do you consider that your child's physicians have provided you with sufficient time?" with the response scale "Never", "Rare", "Often", "Always". Person-duration scales were also used in questions like "For how long did your child's symptoms last until your first contact with a physician?" with the response scale "A few days", "A few weeks", "A month", "2-3 months", "Four months up to a year", "One year or longer". Intensity scales were used for questions like

“Overall, how much do you trust your child's physician?” and “How much information have you received about your child's disease?” and “How much information have you received about your child's treatment?” For these, there were four answering categories “None”, “A little”, “Moderate”, and “Much”. For categorical variables measured with questions like “Do you feel that the physicians gave you the chance to express your thoughts and concerns?”, there were only two answering categories “Yes”, “No”. Some questions concerning the parents, for example if they had received recommendations upon discharge, whether or not the recommendations had been followed, and if the parents found the given recommendations relevant and manageable the response alternatives were: “Yes” and “No”. If any of the recommendations had not been followed, the parents were given five options to provide information on why they had not been followed.

Starting with about 150 questions originating from the interviews, we gradually reduced the number of questions excluding those that resembled one another until we had 89 (*Pre-1*) and 90 (*Pre-3*).

4.2.4 VALIDATION OF QUESTIONNAIRES

To ensure that all questions and answer alternatives were relevant and easy to understand, face-to-face interviews were conducted with 28 parents of children newly diagnosed with cancer at the pediatric oncology wards. The primary aim at this stage was to determine if there was any essential data we had missed (validation of content). Face-to-face validation also gave us the chance to see if some questions or alternative questions were unclear or differently understood by different individuals (validation of interpretation). In order to ensure that neither the subjective opinion of the interviewer nor the comparable opinions of others in the research group would alone guide the choice of question formulation and alternative answers, we encouraged the study population to choose between similar questions and similar alternative answers (validation of choice).

The questionnaires were constructed in English by the team in Sweden, and were then translated into colloquial Egyptian and then back translated to assure a correct and accurate colloquial translation. The questionnaires were translated by a translation company and edited subsequently during the several interview phases.

4.2.5 PILOT STUDY

The questionnaires were validated in a pilot study comprising 54 parents of children newly diagnosed with cancer. The pilot study was conducted at the same three governmental hospitals. During this study, we tested the data

collection logistics, estimated a likely participation rate and checked whether some questions were left unanswered.

We ended up with two study-specific questionnaires; *Pre-1* administered prior to chemotherapy treatment cycle 1 and *Pre-3* prior to chemotherapy treatment cycle 3. In addition, a Case Report Form (CRF) was attached to each questionnaire. The CRF contained the following information: child's name, address, name of parent, age, gender, length, weight, diagnosis, date of interview, scheduled chemotherapy treatments, medicine received and dose.

The questionnaires (*Pre-1/Pre-3*) contained 89 and 90 questions respectively and were divided according to the following topics; *Pre-1*: socio-demographic data, cancer diagnosis, family history, the amount of information provided about disease, treatment, and most common side effects of treatment, hospital stay experience, diagnosis disclosure, communication with physicians and health care professionals, and psychosocial and emotional experiences. *Pre-3*: reasons for delay to medical treatment, information provided by health care professionals, investigations, hospital stay experience, next treatment cycle attendance, adherence to medical treatment at hospital and home, psychosocial and emotional experiences, and trust in physician and other health care professionals as well as the medical care.

The questionnaires were marked with a serial number on the back and could only be decoded by the researcher.

4.3 METHODS OF DATA COLLECTION

All parents in our study population were approached at the daycare center or at the pediatric oncology ward on the day they came to the hospital to start their child's first chemotherapy cycle, which was considered our baseline. They were informed about the study, asked to give their consent to participate, and, if they agreed, asked to fill in our first questionnaire (*Pre-1*). The same parents were subsequently approached and asked to complete the second questionnaire (*Pre-3*) when their child came to start the third chemotherapy cycle. We excluded parents to children admitted for surgery and radiation therapy, as they did not fit the inclusion criteria. Due to the high illiteracy level in Egypt, the study team decided to have an interviewer administer the questionnaires; reading the questions out loud and then filling in the spoken answers by writing the answers in the questionnaire.

4.4 DATA ENTRY

Data were manually entered into Epidata version 2.0 and 20 percent of the questionnaires were re-entered to check accuracy. The program is pre-programmed to identify possible false entries, like inappropriate values, in order to minimize bias. All doubtful answers such as double-marked, written notes on the side were referred to the principal investigators. Having an interviewer filling in the questionnaires, significantly reduced errors such as wrong marks or missing a question. Furthermore, 45 randomly chosen questionnaires were re-entered to test the reliability of data entering.

4.4.1 STATISTICAL ANALYSES

The relative risks (RR) with corresponding 95 percent confidence interval were calculated as the ratio of the percentages of each category of the independent variable using the SAS procedure freq with option relrisk. For calculating adjusted relative risks with corresponding 95 percent confidence interval, a log-binomial regression model was performed. To find predictors for an outcome, we included possible variables in a model, and automatic selection was performed utilizing the SAS procedure logistic with selection options backward and forward and default settings. As a complement, we also performed model selection using Bayesian model averaging (BMA) on imputed datasets created with multiple imputation by chained equations (MICE). Also, we used Chi-square goodness of fit test or, where appropriate, Fisher's exact test, to produce a *P* value that illustrates whether there is a difference in proportions between two groups. A *P* value below 0.05 was considered to indicate statistical significance. For BMA, a posterior probability of 95 percent indicates a strong evidence for association.

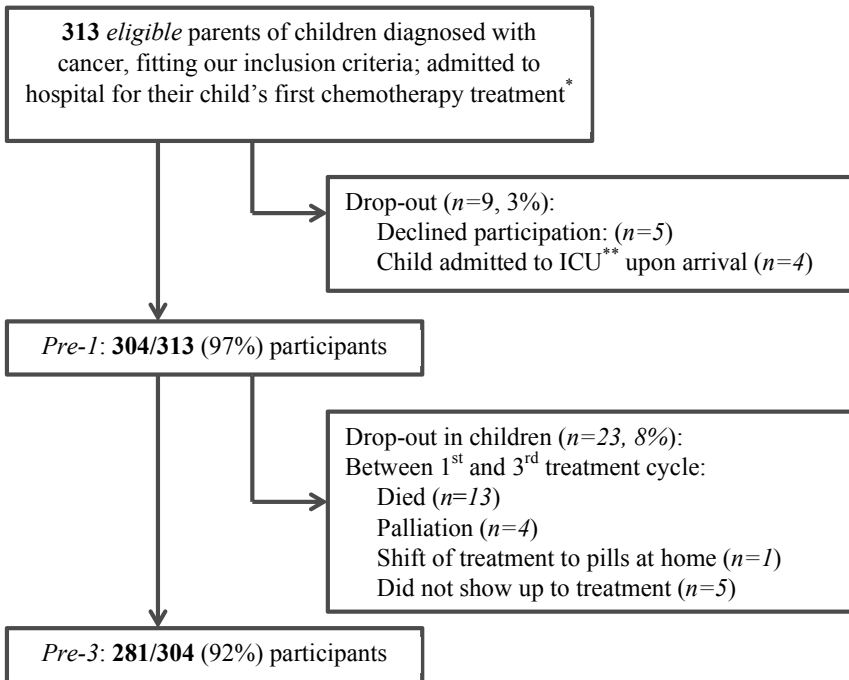
All statistical analyses were performed by a statistician using software SAS version 9.3 for Windows (SAS Institute Inc., Cary, NC, USA) and two packages (MICE/BMA) in the freeware R (R: A Language and Environment for Statistical Computing; 2005). See manuscript I-IV for details of statistical analyses in each study.

5 RESULTS

5.1 PARTICIPATION RATE AND OVERALL CHARACTERISTICS

Among the 313 eligible parents, 304 (97%) answered the first, and 281 (92%) the second questionnaire (figure 5). The study population comprised one parent of every child. Five years after the study was conducted, we had a survival follow-up and we found that 58 percent (176/304), with an additional 10 percent ($n=30$) of lost to follow-up, were alive (Figure 5). For further details of the study group's characteristics, see Table 1 in Paper I-IV.

Figure 5. Study population



* One parent of every child

** ICU: Intensive Care Unit

The majority of children had both parents as primary caregivers (84%), but the mother was the accompanying parent during the hospital stay (81%). One-third of the mothers (35%) and the fathers (32%) did not have any education, whereas about 10 percent had a university degree. The vast majority of the mothers (90%) were housewives, and the fathers were laborers (67%). Most of the families lived in rural areas (66%).

5.2 PAPER I

The basic goal of the research for the first paper was to investigate predictors of trust in the health care professionals and the medical care as reported by the parents of the children diagnosed with cancer. Parents' trust in the medical care at the time of the child's third chemotherapy cycle was significantly associated with the following at the start of treatment: having received at least moderate information about the disease (RR 13.2; 95% CI 7.8–22.3) and the treatment (RR 17.2; 95% CI 9.5–31.4), having the information provided in an adequate manner (RR 13.7; 95% CI 7.8–24.1), having the opportunity to communicate with the child's physicians (RR 21.3; 95% CI 11.7–38.8), being given the chance to express thoughts and concerns with the physician (RR 5.9; 95% CI 2.9–12.1) and with the nurses (RR 4.8; 95% CI 2.4–9.5), being satisfied with the physician's conversation style (RR 30.6; 95% CI 14.4–64.9), having the emotional needs met (RR 22.2; 95% CI 11.8–41.9), and being met with care by the child's physicians (RR 32.0; 95% CI 15.2–67.7). After adjusting for all independent variables addressed above, using forward and backward stepwise regression, six independent variables remained to explain our main outcome (trust in the medical care provided to the child): information received about the child's disease ($P=0.0251$), information received about the child's treatment ($P=0.0064$), opportunity to communicate with the child's physicians ($P=0.0203$), being satisfied with the conversational style of the child's physicians' ($P<0.0001$), perception that the child's physicians were sensitive to the parent's emotional needs ($P=0.0031$), and finally considering that the child's physicians had met the parent's with care ($P<0.0001$). However, by using a more strict model selection according to BMA, only one of the independent variables fulfilled the posterior probability limit of strong association ($>95\%$), namely regarding that the child's physicians had met the parents with care (95.4%). Among parents who were met with care by the child's physicians to only a little or no degree at the start of treatment, not a single parent reported much degree of trust in the medical care provided at the time of the third chemotherapy cycle.

5.3 PAPER II

The goal of the research for the second paper was to address the rate and pattern of disease disclosure to parents of children newly diagnosed with cancer at the Children's Cancer Hospital in Egypt. To do this, we examined in some detail the nature of disease disclosure at the time of the first chemotherapy treatment, when the child has already been diagnosed and is about to start chemotherapy treatment. We found that nearly three quarters (72%) of the parents had their child's cancer diagnosis communicated by the physician. Only 39 percent of the children were present during the disease disclosure conversation. The majority

of the children were between the age of 5 to 18 (55%) and 45 percent were between 0 to 4 years old. During disease disclosure, physicians used “tumor” (the Arabic word is *waram/swelling*) most commonly to describe the disease ($n=292$). The second most common term used was “difficult disease” ($n=161$) whereas “malignant disease” ($n=31$) and “cancer” (the Arabic word is *saratan*) ($n=18$) were less frequently used terms. The majority of the physicians stated the cause of the child’s malignancy as “unknown” ($n=110$), or due to “divine” reasons ($n=100$). A few parents were also given the information that their child’s disease was caused by “heredity” ($n=8$) and “environmental factors” ($n=1$). There were no statistically significant associations between psychosocial and demographic characteristics and by whom the disease was disclosed.

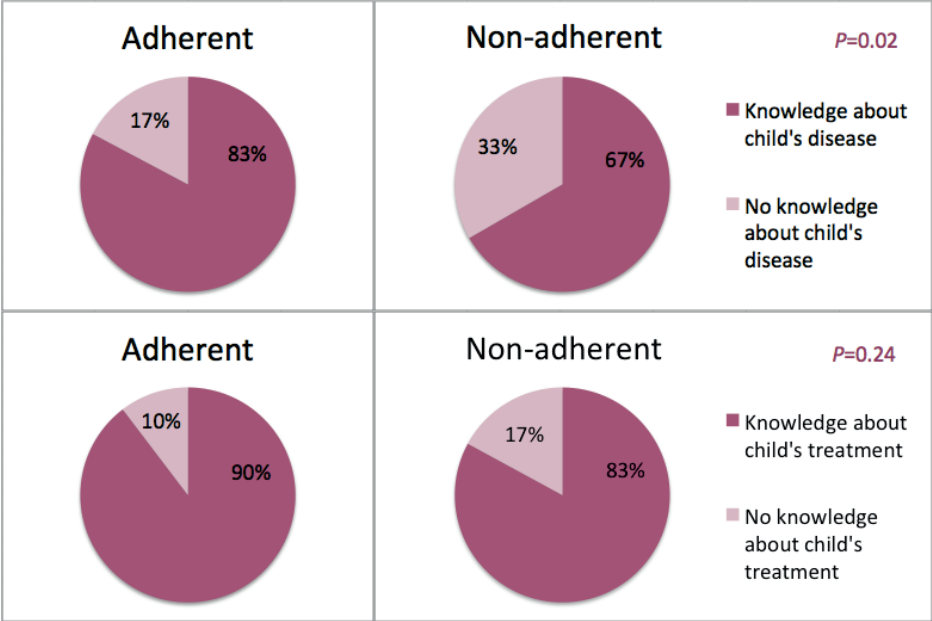
5.4 PAPER III

The aim of the research on which the third paper was based was to investigate the rate and pattern of adherence and the predictors of non-adherence to the medical recommendations that are provided to the parent and child upon discharge. More than two thirds of the children admitted to their third chemotherapy treatment received medical recommendations upon discharge from their second chemotherapy treatment. In the studied population, which had a total of 281 parents after drop-out between the two questionnaires; 64 percent ($n=181/281$) of the parents had reported that they received medicine to take home upon discharge between the first and/or second chemotherapy treatment. No statistically significant differences were found between the two groups of parents who followed ($n=58/181$, 32%) and who did not follow ($n=123/181$, 68%) the medication plan except for an increased adherence among children of educated mothers ($P=0.017$). Among the adherent children’s parents, 88 percent ($n=51/58$) reported difficulties following the recommendations, whereas almost all parents ($n=56/58$, 97%) thought the recommendations were relevant. According to the parents’ reports, $n=111/123$ (90%) of the children who received medical recommendation upon discharge refused to take the provided medicines while at home. Furthermore, 81 percent ($n=100/123$) of these parents reported that the information provided upon discharge was insufficient. In addition to our data reported in the manuscript, an additional finding was found in a comparison of the adherent and non-adherent parents at the time of their child’s third chemotherapy. We found a statistically significant difference concerning reported knowledge about the child’s disease (adherent 48/58, 83%, and non-adherent 82/123, 67%, $P=0.02$). On the other hand, no statistically significant difference was found between the groups’ reported knowledge about treatment (adherent 52/58, 90%, and non-adherent 102/123, 83%, $P=0.24$) (Figure 6).

In the adherent group one out of five parents ($n=12/58$, 20%) reported trust in

their child’s physician while 8/58 (14%) reported trust in the other health care professionals. Corresponding numbers for trust among non-adherent were 8/123 (7%) for both the child’s physician and other health care professionals. Nearly all parents ($n=122/123$) who received medical recommendations upon discharge, but who were non-adherent, reported an intent to attend their child’s next chemotherapy treatment cycle, although the majority in this group did not consider the treatment to be of any use, $n=180/277$ (65%). After adjusting for seven independent variables to explain the parents’ intentions to pursue the next chemotherapy treatment cycle, two independent variables were left to explain that outcome: doing so for the sake of their child’s life (70%) ($P=0.005$) and worry that their child would die if they discontinued the treatment (81%) ($P<0.0001$). No parent had been involved in the decision making regarding the child’s treatment or hospital care and 94 percent ($n=266/281$) of the parents reported that they had no or little knowledge about their child’s disease and treatment. Nine independent psychosocial and emotional predictors were identified and included in a model. The risk of not having the psychosocial and emotional needs met in the non-adherent group was almost double the risk in the adherent group. Furthermore, the non-adherent group of parents reports the situation as being more than five times more difficult to manage than those who adhere.

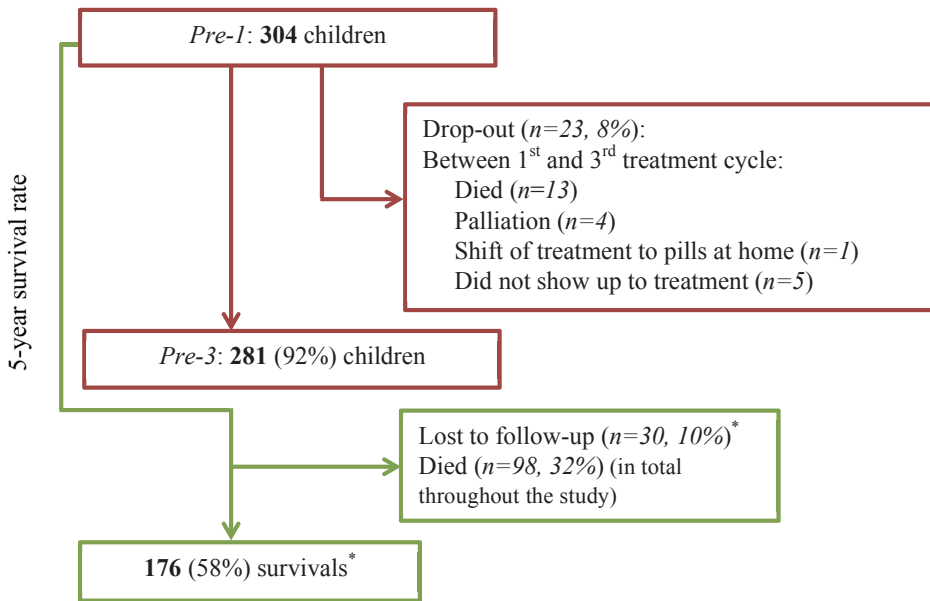
Figure 6. Adherent and non-adherent parents’ reported knowledge about disease and treatment at the time of their child’s third chemotherapy cycle



5.5 PAPER IV

The overall aim of the fourth paper was to investigate predictors of mortality in pediatric malignancies and to investigate the present mortality rate at the Children’s Cancer Hospital in Cairo, Egypt after a five-year follow-up in the study group. We considered the various psychosocial predictors addressed in the questionnaires such as late to treatment, adherence and non-adherence to medication, trust and information provided. We also considered BMI, age, gender, and diagnosis and residence area. Five years after the study was conducted, we found that 58 percent ($n=176$) of the children had survived the first five years after treatment initiation (Figure 7). Thirty children (10%) had no current active status at the hospital, and therefore, are lost to follow-up. The majority of the children were in the age group 0-4 years (44%) and males (59%) dominated. The majority of these children had a leukemia ($n=131$) followed by lymphoma ($n=49$), neuroblastoma ($n=28$), sarcomas ($n=25$) or brain tumor ($n=17$). The leukemia (73%) and lymphoma (73%) patients had the best prognosis.

Figure 7. Survival among children followed up for five years



* The survival rates are likely to be between 58% and 68% due to 10% of lost to follow-up

Moreover, we found a statistically significant difference in the mother’s level of education between the group that survived and the group that died (Table 4). No statistically significant differences were found between the groups in relation to

several demographic factors such as age, gender, BMI, residence, the father's level of education and occupation of both parents (Table 4).

Table 4. Demographic factors versus survival/non-survival

Demographic factor	No./total no. (%)	<i>P</i> value*
Gender		
Male	103/163 (63)	0.66
Female	73/111 (66)	
Age		
0-4	78/124 (63)	0.08
5-8	39/57 (68)	
9-15	46/79 (58)	
16-18	13/14 (93)	
BMI		
Normal	102/148 (69)	0.57
Underweight	37/59 (63)	
Overweight	10/16 (63)	
Obese	12/15 (80)	
Geographical area		
Urban	61/90 (68)	0.57**
Rural	113/180 (63)	
Abroad	2/4 (50)	
Mother's level of education		
University	58/75 (77)	0.02
Non-university	65/106 (61)	
No education	53/93 (57)	
Father's level of education		
University	58/78 (74)	0.09
Non-university	65/104 (63)	
No education	52/89 (58)	
Mother's occupation		
Employee	11/16 (69)	0.68**
Laborer	7/11 (64)	
Own business	0/1 (0)	
Housewife	158/246 (64)	
Father's occupation		
Employee	43/57 (75)	0.16
Laborer	117/186 (63)	
Own business	6/12 (50)	
Unemployed	8/15 (53)	

* Chi-square goodness of fit test

** Fisher's exact test

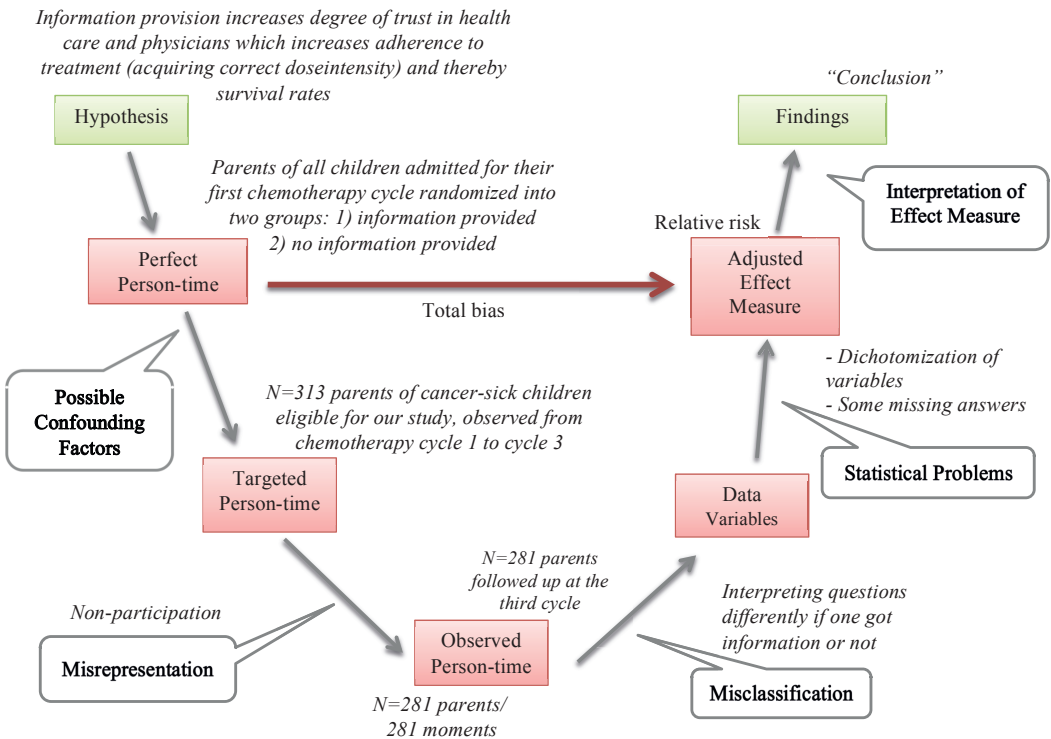
6 DISCUSSION

6.1 METHODOLOGICAL CONSIDERATIONS

6.1.1 VALIDITY

The validity of a study refers to the extent to which the effect measures correspond to reality. I have made an effort optimizing the validity of the effect measure in this thesis. “The perfect study” does not exist as our real-life studies are flawed by either systematic errors, which introduce bias, or random errors that influence the precision of the study. At our division we utilize epidemiological methods for study design and data interpretation adapted to the cancer field according to the hierarchical step-model for causation of bias [53,54,55]. This model describes how the final, adjusted effect measure deviates from the “perfect study”, the counterfactual situation. The model proceeds in four steps from the “perfect person-time” towards a calculated, often adjusted, effect parameter (Figure 8).

Figure 8. A hierarchical step-model for causation of bias applied to our study



6.1.2 STEP 1: CONFOUNDING

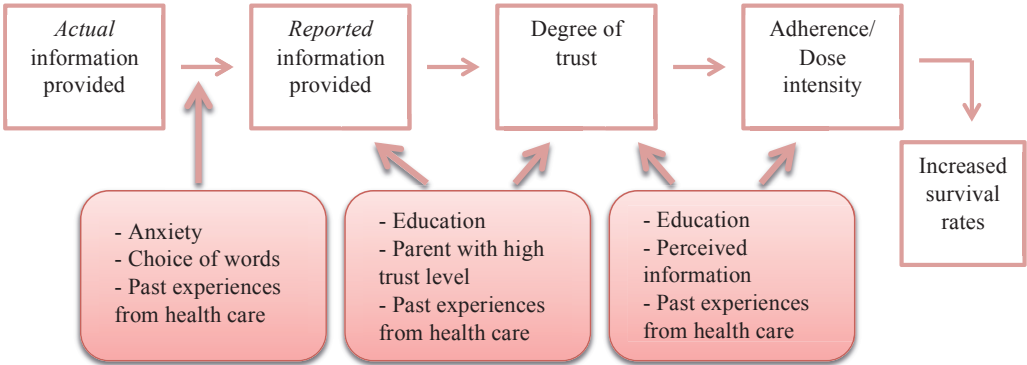
In the hierarchical step-model, the counterfactual situation is described as the “perfect person-time”. For obvious reasons, this situation is unattainable; therefore we strive to find an appropriate “targeted person-time” that would support valid conclusions. Shifting from the “perfect person-time” to the “targeted person-time”, the first step in the hierarchical step-model, introduces errors known as giving confounding. Confounding occurs when an effect-measure deviates from the null due to a factor other than the exposure we study; the factor is associated with the exposure and is an independent risk factor for the outcome. Having the means to control confounding is of central importance for an epidemiological study [58]. In our study, we reduced the risk of confounding by including all parents and children newly diagnosed and admitted for the first chemotherapy cycle. We also included in our analyses several questions on possible confounders such as age, gender, BMI, education, occupational and demographic status.

In paper I, on information provision and trust, a possible confounder for which we had no information, is the presence of parents who already display a high degree of trust. Such a group could confound the association between the parents’ perception and the amount of information provided and hence the amount of trust they report. Other possible confounders could be the parents’ past experience with health care, for which we have no data, as well as their educational level, which showed no statistical significance. In addition, the lack of information regarding the parents’ religious beliefs and ethnicity is a possible limitation. However, we did not find any associations between regions (as a surrogate for ethnicity) or any other socio-demographic factors. In paper II, on cancer disclosure, confounding is not a strong issue because the paper is descriptive and does not deal with causal relations. In paper III, on adherence to prescribed medication, the main confounders we addressed are the amount of information provided, educational level, and the parents’ past experiences with health care. Yet, we have no data regarding the parents’ past experiences with health care. Also, we found increased adherence among educated mothers ($P=0.017$) so, there could be an association but we do not believe the evidence is strong enough. Also, we did not find any association between region (as a surrogate to ethnicity) and any other socio-demographic factors and thus we believe that these factors probably did not confound our reported associations. This paper partially supports our main hypothesis that information about the child’s disease and a higher degree of parental trust has an association with child’s adherence to treatment, yet we could not find an association between adherence to medication while at home and increased survival rates. In paper IV on five-year observed survival rate, we did not find any apparent confounders. Given the availability of sufficient medication and accurate follow-up, it is

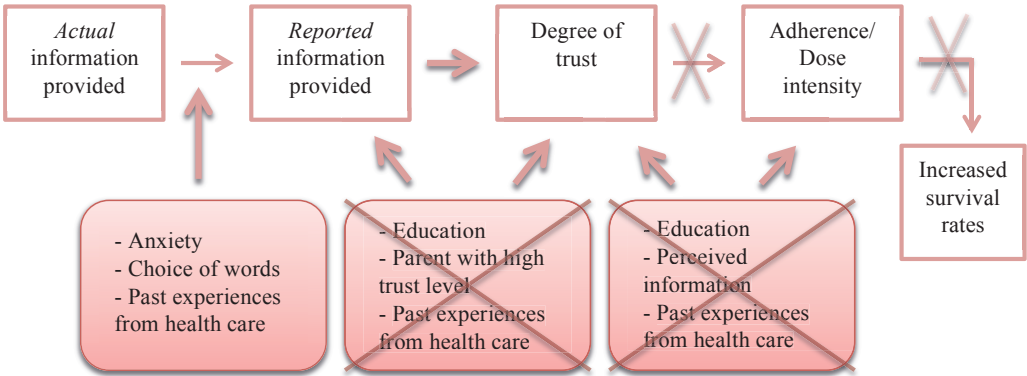
unlikely that death could have resulted from other matters unless the child had complications resulting from other diseases that he or she had before cancer diagnosis or the death might have occurred as a side effect from the chemotherapy provided.

Figure 9. Mechanism for the main hypothesis of the study

A. Hypotheses prior to the thesis



*B. Some thesis findings**



*After additional analysis, we found a statistically significant association between the amount of information provided about the child’s disease and adherence.

6.1.3 STEP 2: MISREPRESENTATION

When shifting from the “targeted person-time” to the “observed person-time”, the second step in the hierarchical step-model, systematic errors may be introduced due to non-participation or lost to follow-up. In our study, we had a

relatively large study-population and a high participation rate (97% in *Pre-1* and 92% in *Pre-3*), which should reduce the risk of selection-induced systematic errors. The dropout between the two questionnaires was due to shift of treatment/palliation $n=5$, death of child $n=13$ and not showing up $n=5$). We have an additional 10 percent lost to follow-up in paper IV where five-year observed survival rates were included. We can only speculate about the circumstances among those lost to follow-up. This is a limitation, though it is expected in this part of the region where follow-up is not as accurate and mandatory as in the Western countries.

6.1.4 STEP 3: MISCLASSIFICATION

Incorrect information due to measurement errors can cause systematic errors when shifting from the “observed person-time” to the “data”, the third step in the hierarchical step-model. Measurement errors could concern both the exposure and outcome under study and can be differential or non-differential. Differential misclassification is dependent on and varies with either the exposure or the outcome, whereas non-differential misclassification is independent of these two measures. Therefore, non-differential misclassification is expected to shift the effect measure towards 1.0, i.e. no effect, while differential misclassification can affect the effect measure in any direction. We tried to diminish the risk of misclassification by repeated interviews with the parents of the cancer-sick children who were going through the same type of treatment, taking their perspective into account when constructing the questionnaires, using simple language and testing the questionnaires for face validity, participation rate and response rate to single questions before conducting the main study and having an interviewer administering the questionnaires. Also, administering the questionnaires right before the initiation of treatment and right before the third treatment cycle was believed to control for memory-induced problems. However, we cannot avoid the risk of misclassification completely. Inadequate entering of data into the computer software could result in misclassification, thus, a random selection of 20 percent of the questionnaires were re-entered to check accuracy. In paper I, on information provision, misclassification can occur due to the over-or underestimation when reporting the amount of information received by the physician. However, it is more likely to estimate correctly as the questionnaires are distributed shortly after the diagnosis is made and right before the first chemotherapy cycle. In paper IV where five-year observed survival rates were extracted, we could not control for any mistakes that this procedure might have brought about when extracting the data. Errors like mistaken classification of diagnosis could have also occurred. We had one person extracting the five-year survival data and we did not have a re-examiner of the final extracted data that might have caused systematic errors.

6.1.5 STEP 4: ANALYTICAL ADJUSTMENT

Random errors are conceived as those errors that remain when systematic errors have been eliminated. Such errors are unpredictable and have null expected value i.e., they are inconsistently scattered around the true value. Statistical significance is used to test whether or not a result is likely to have occurred by random chance. In our analysis, we considered an effect measure to indicate a statistically significant difference when its 95 percent confidence interval did not cover 1.0. Moreover, a P value below 0.05 in a statistical test was considered to indicate statistical significance.

7 GENERAL DISCUSSION

7.1 PAPER I

To be met with care by the child's physician at the time of entry to the first chemotherapy cycle was the most important predictor for the parents' subsequent trust at the time of their child's third chemotherapy cycle. In a review by Hall et al., it was suggested that patients who trust their physicians are more likely to perceive results of treatment in a positive manner, and this in turn brings about a more positive view of the future [25]. Trust is thus considered a key element for strengthening the patient–physician relationship and also ensuring patient adherence with recommendations [59]. Providing high-quality information regarding the child's cancer disease, treatment, and prognosis in an understandable and adequate manner has proven to be important for the parents' satisfaction regarding the quality of care [60,61,62,63]. Interestingly, we found in our study that the parental trust in the physician and the medical care was not related to the amount of information given to the parents of children with cancer, after adjusting for factors related to how the information was provided and how the parents were regarded during the information sharing. Thus, our data indicates that it is the manner in which health care professionals communicate, rather than exactly what is communicated, that creates trust in the physicians, the nurses, and the medical care. Our results are supported in the literature, where the strongest predictor of trust has been reported to be the physician's personality and behavior [25]. Not surprisingly, the physician's conversational style was among those factors that were clearly determined to be a predictor of the subsequent level of trust among parents. In other words, it is not what you say, but how you say it that matters. To have the opportunity to communicate with the child's physicians was one of the strongest predictors of trust in our study.

Clearly, there is room for improvement regarding patient–physician communication. Physicians need to listen to the parents and assess their understanding and allow space for silence and questions as part of information sharing. Several studies indicate that the majority of the parents of children with incurable cancer do want to know the truth about the disease and the prognosis [63,64] and that this information by no means make them less hopeful [64]. Therefore, it is important that children are properly informed prior to medical investigations and treatment initiation. Children, especially, are in need of information to help them cope with their imagination and to separate reality from fantasy. This information sharing, however, needs to be adapted according to the parents' and the child's preferences, which in turn depends on the child's age and level of understanding [65]. Having a disrespectful and arrogant attitude

and giving information in an insensitive manner negatively affects the level of satisfaction with, and trust in, care expressed by parents with children in palliative care [31]. Receiving emotional support, not least from the patient's physicians, is considered crucial for patient satisfaction [66]. Indeed, in our study, the only factor that remained significantly associated with trust after multivariable adjustment was "being met with care by the child's physicians".

In conclusion, our data indicates that it is the way health care professionals communicate rather than what is communicated, that creates trust among parents. We found that parents who considered that their child's physicians had met them with care at the beginning of their child's treatment trusted the medical care given at the time of the child's third chemotherapy cycle to a significantly greater degree than did other parents.

7.2 PAPER II

We found that nearly three quarters (72%) of the parents had their child's cancer diagnosis communicated by the physician, whereas the rest (28%) had the cancer diagnosis disclosed by others. Only 39 percent of the children were present with the parent or parents during the disease disclosure conversation. On the other hand, 45 percent of the present children were between the age of 0 to 4 and 55 percent were between the age of 5 to 18. Naming the disease at the point of disease disclosure was equally controversial as illustrated by the preference of physicians for using the designation "tumor" ($n=292$). The Arabic word for "tumor" ordinarily refers to the presence of a swollen area and is not associated with a malignancy/cancer to the same extent as in the Western society. We assume that, even if many parents and children may be present during presentation of information by the physician, they may not understand what they are told or what is really meant by having a "tumor".

Barriers to disclosure are many and vary across cultures and societies. Bedikian et al. conducted a survey regarding the experience of 249 physicians in Saudi Arabia, which revealed that 75 percent of the physicians preferred disclosing the diagnosis to close family members rather than the adult patient [67]. Another study from Saudi Arabia revealed that physicians expressed the wish to inform patients of the diagnosis but they did not know what to say or how to say it [41]. They expressed worries that breaking bad news could evoke fear and anxiety in patients, which they wished to avoid, and they may also be concerned that the patient may not be able to cope with the difficult news [41]. In addition, one Turkish study identified the relatives of cancer patients as one of the most significant barriers to disclosure [43]. Another study from Saudi Arabia revealed that relatives to cancer patients believed that disclosure of the cancer diagnosis to the patient could be harmful and bring about suffering for the patient [40]. Furthermore, in a cross-sectional study conducted in Pakistan where 147 cancer

patients participated, 83 percent ($n=63$) of the patient's family members did not allow the patient to be informed of his or her diagnosis [42]. Similar attitudes were found in a study in Turkey where almost half of the family members (130/270) refused to allow disclosure of the disease to the patient [43]. Though disease disclosure is controversial, and even though several studies from the Arab World indicate that the barriers to disclosure are due mainly to the physician's preferences and/or the relatives of the patients, it is notable that nearly three quarters of the parents in our study group were told the diagnosis of their child. There has been a positive tendency of improved disease disclosure in the Arab World and the attitudes have shifted for as yet unknown reasons. In the Bedikian et al. survey of 100 adult cancer patients and next of kin in Saudi Arabia in 1984, only 16 percent of the patients were told that they had "cancer" and 34 percent were told they had a "tumor" [67]. On the other hand, 69 percent of the next of kin were told about the diagnosis of cancer [67].

The diagnosis of childhood cancer is very dramatic and the associated anxiety and stress level are repeatedly addressed in the literature [68,69]. Thus, communication ought to take place on several occasions since what is very hard to talk about at first may get easier over time, and what can be shared and heard at first may expand, as everyone is ready for more detailed information at later stages. Furthermore, the variation across nations is great in terms of the prevailing cultural assumptions and the ethnic context of the family, the family dynamics, the family size, the family structure, the age and educational level of the child, as well as the resources and abilities of the parents, the children and the health care team involved, all factors need to be taken into consideration [68]. Also, children and parents have different needs and we must ask patients at each consultation what those needs are [70]. Several studies have addressed the patients degree of desire of disease disclosure, such as the study made by Butow et al. where 85% of the patients reported that they wanted a large amount of detail of their disease and 15% wanted minimal detail [70]. All parents in our study group reported a wish for more information about their child's disease and treatment, thus, we argue that even though there might be a variance in desire of the degree of information the patient may have, the parents of the child should be told all the details of their child's disease and treatment and they should be involved in the decision-making. Moreover, effective communication serves not only the patient and family members, but also enables the physician to improve the patient's understanding of his or her disease, improve patient adherence to treatment regimen, use time efficiently and avoid burnout [71]. Effective communication is responsive to the needs of the whole patient and family dynamics; it is essential to patient-centered and family-centered care, the basic building block of the medical home concept, which is endorsed by the American Academy of Pediatrics (AAP) as a cornerstone of care [72]. Taking time to build

rapport and understand the child and family builds trust, leading to increased reporting of the actual reason for the visit and influences treatment adherence and outcome, adaptation to disease, and bereavement [72]. Clearly, improved communication will enhance patient outcomes and satisfaction [72,73].

Considering that truth telling about one's diagnosis is the first step towards good patient-physician communication and the first step for treatment decision-making in cancer patients, it is evident that common practice in the Arab World stands in the way of such communication. Widespread acceptance of full disclosure is hardly to be expected in the near future due to cultural differences and social dynamics in different regions of the Arab societies and the question is if there are regions in these societies where change might take place relatively rapidly. However, there is no doubt that there is a need for greater recognition of patient autonomy among physicians and the need for developing better practice for the disclosure of cancer diagnosis to the patients. Also, to advocate for the patient's ethical rights to know and share in the decision making of his or her disease.

7.3 PAPER III

Sixty-eight percent (123/181) of the parents to children who received medical treatment upon hospital discharge report that their child did not comply with the treatment. In this group, the child's resistance was the main predictor for non-adherence as well as lack of information provided to parents. Our findings are supported by Kondryn et al., who found that between 27 and 63 percent of adolescent patients did not follow the prescribed oral treatment [51]. One third (32%) of this group of children was between 9 and 15 years old. Age appears to play a role in adherence-related behaviors in children with cancer [50,74]. As children grow, behavioral concerns related to adherence may become dominant for some children who may actively refuse medication [50]. Also, as children become more autonomous, adherence tends to become more difficult to maintain [49]. Adolescents usually strive for autonomy and independence and usually have limited ability to understand the consequences of their actions, and thus they become frustrated with parental authority and the limitation in their life due to their disease and treatment, all which may lead to non-adherence [50]. Furthermore, adolescents' oppositional behavior and wanting to be like their healthy peers has been documented as a reason for non-adherence [49]. Side effects of treatment could be another reason; yet, we have no data from our study to investigate such an effect.

Furthermore, previous studies have found that poor adherence among children is mainly due to their own and their parents' lack of knowledge and understanding about the disease and its treatment [48,50]. This goes in line with our finding in

this paper, where the adherent group had more knowledge about their child's disease in comparison to the non-adherent group and where the majority of the children above the age of 5 had not been part in the disease disclosure conversation (Paper II). A child can tolerate discomfort if he or she is prepared for it, understands its real purpose and receives adequate support from understanding adults. Parents also need information, since their emotional stability is necessary for the child's psychological well-being. In our study, we found that inadequate information provided to the parent was an important predictor for non-adherence to the prescribed medical regimen. Clearly, communication between the health care providers and the patient is an important factor for adherence [50]. When patients understand their physicians they tend to follow their treatment regimen and modify their behavior to a larger degree [75]. Furthermore, in a study made by Safran et al., trust was found to be a key element in the patient-physician relationship and older patients who trust their physician were among those who complied best with the medical regimen [58]. We have previously reported a lack of trust in the child's physicians and the health care professionals in our study group (Paper I). We can now show that adherence to medication while at home was more commonly reported in parents who trusted the physicians and the health care professionals (Paper II). Furthermore, Perez-Carceles et al., conducted a cross-sectional survey at an urban Spanish university hospital of 300 patients admitted to the emergency department during a period of three months [76]. They found a significant relation between perceived information to the patient and his or her satisfaction with the care [76]. These data are supported by our previous findings that parental satisfaction depends upon the quality of communication with health care professionals (Paper I).

Taking time to understand the child and family builds trust, leading to increased reporting of the actual reason for the visit and influences treatment adherence and outcome, adaptation to disease, and bereavement [72]. Nonetheless, several studies within the field of psychology and psychiatry have observed that psycho-education and the provision of information are most effective when aligned with behavioral and problem-solving strategies to enhance and promote adherence [28,77,78,79]. Adherence to oral chemotherapy in childhood malignancies is a complex, multidimensional behavior that requires understanding on the part of the parent and child and also requires that they correctly carry out complex instructions from the health care provider about a variety of medications. These instructions take into account factors including the time of the day when the medication is to be administered, whether the medication must be administered by restricting intake of certain products such as dairy products or must be taken on an empty stomach. All these factors may require frequent dose adjustments in response to blood counts, infections, clinical course, or changes in weight or body surface area. Therefore, adherence involves not only a willingness to

follow the regimen over a prolonged, defined period, but also the cognitive competence and psychomotor skills to carry out the process. Hence, the role of the parents in supporting, guiding and aiding their child is crucial.

7.4 PAPER IV

Among the 304 children diagnosed with cancer at Children's Cancer Hospital in Egypt, 281 children were followed up after five years and we found that 58 percent ($n=176$) had survived five years after treatment diagnosis with an additional 10 percent lost to follow-up. Thus, the survival rates in our study group have increased considerably in comparison with the rates estimated (between 20% to 30%) by the NCI Egypt and WHO in the past [10,20,80] and before the new hospital started running. These survival rates are not yet comparable to the estimated rates in Western countries; nevertheless, they only reflect our study group and not the general overall rates of the entire hospital.

Various obstacles are addressed in the literature accounting for the high mortality rates in this part of the world. Among others, inadequate access to medical care, lack of education and knowledge in seeking health care, long distance transportation and limited access and absence of effective chemotherapy drugs [10]. These challenges have to a large degree been overcome at the Children's Cancer Hospital in Cairo in various ways. Major awareness campaigns have been broadcast all over the country regarding prevention, detection, dietary awareness and seeking health care as well as defeating the stigma attached to cancer and bringing hope to people by informing them about the effective treatment that the hospital offers by engaging the treated and cured children in the ads.

Probable explanations of the relatively increased survival rates at the hospital could be the overall cancer treatment provided (chemotherapy, radiation, surgery and physiotherapy) that corresponds to the US protocols with modifications tailored for the children in Egypt as well as the a multi-speciality ward at the hospital that offers a wide range of specialists. This service has helped in controlling and avoiding health complications for the child as the specialists have access to the child's medical records and can prescribe medication that does not have a synergistic effect on the child's cancer treatment. This service has certainly saved the parents' money and time and provided convenience and encouraged health care seeking as well as brought about effective health care provided to the child.

In addition, one of the major prior concerns regarding survival in childhood cancer in Egypt has been the long distance between the child's home and the hospital and the lack of transportation to hospitals among rural inhabitants [10,20]. Interestingly, we found no difference in survival rates during the five-

year follow-up between urban (68%, 61/90) and rural (63%, 113/180) residents. This could to a certain degree be explained by the offered transportation allowance that the parents are offered to/from the hospital as well as the housing alternatives offered during treatment if the child lives too far away from the hospital or if he or she is too tired to travel back home. Furthermore, the hospital has established a welfare foundation for financial assistance and for other types of compensations such as loss of or decreased salary due to reduced working hours/days when the parent is at hospital for treatment of the child.

We found an association between information and the way it is provided with trust and adherence to medication, yet none of these predictors were related to survival in our study group except for mother's educational level. We also investigated other psychosocial and demographic factors along with other factors related to the child (gender, age, BMI) to find out if any of those predictors are related to survival and none of them turned out to be predictors. Therefore, our hypothesis was refuted as no statistically significant differences were found between the group that survived and the group that died in relation to psychosocial predictors addressed above.

The Children's Cancer Hospital may not be representative of the quality of care that is found in other hospitals in Egypt or the rest of the region, although it is free of charge like any governmental hospital. Hence, the overall mortality rates in Egypt will probably not decrease more since the hospital only accommodates one-fourth of all patients in the entire country.

8 CONCLUSION

This thesis provides psycho-oncological knowledge about children diagnosed with cancer in Egypt. The main aim of the research on which this thesis is based is to explore predictors of the high mortality rates predicted among these children in Egypt.

We found that:

- Parents reported a higher degree of trust in the health care provided and in their child's physician if they were met with care. Also, having received information concerning the diagnosis and treatment was associated with higher trust in the health care provided and in the physicians. The majority of the parents did not, however, receive information about the disease and treatment.
- Disease disclosure is common among our study group where 72 percent of the parents did receive their child's diagnosis from the physician. Yet, only 39 percent of the children were present during the conversation. Nevertheless, the use of medical terms and possible colloquial equivalents in disclosing the information to the parent is controversial, as the terms used do not clearly convey the nature of the disease.
- Non-adherence to prescribed medication while at home is common among our study group (68%) and two main predictors reported by the parents were child's resistance (90%) and inadequate information provided to the parents (85%). The adherent group reported more knowledge about their child's disease in comparison to the non-adherent group (adherent 48/58, 83%, and non-adherent 82/123, 67%, $P=0.02$). Among the non-adherent group only 8/123 reported trust in their child's physician and health care professionals.
- The five-year survival rates among our study group are compared with the current statistics (58%) with an additional 10 percent lost to follow-up; nevertheless, we could not relate the surviving or non-surviving groups to any of the psychosocial predictors addressed in this thesis.

In this thesis I argue that the patient-physician relationship is an essential factor affecting the nature of the care provided and ultimately the evaluation of the quality of care. This relationship is influenced by a number of elements, some of which are addressed in this thesis. It is apparent from our data that parents to cancer-sick children do not differ markedly in thoughts, feelings and actions

regardless of cultural, religious, or technology advancement. Nevertheless, we find in our study group that the main concerns about the patient–physician relationship remain. This relationship entails a range of mutual responsibilities that include respect, open and honest communication, and trust. It also entails acknowledging and encouraging the parent’s desired involvement in the care, the process of disease disclosure, and the adherence to prescribed medication regimen while at home as well as the obstacles the parents encounter in that. Despite the fact that we did not find an association between psychosocial elements and mortality, we could, however, report numerous psychological and social needs that the parents have addressed.

Apparently, the financial incentives the hospital is offering children of low-income families play an important role in encouraging as well as enhancing adherence to treatment at the hospital at least as concerns the parents in our study group who were compliant with the treatment schedule on a large scale so that lateness to treatment was not an issue.

9 FUTURE PERSPECTIVES

The findings presented in this thesis could be seen as just one step, but a necessary step, towards providing better psychosocial and psychological health among the children diagnosed with cancer and among the parents of these children in Egypt.

The Children's Cancer Hospital (CCHE) is unique and has brought about a noticeable improvement in the level of cancer health care in Egypt. Nevertheless, in reality, CCHE does not provide for the majority of the children in Egypt as it annually accommodates only one-fourth of all diagnosed children. Despite the fact that the situation for the children and their parents at CCHE is different from that at all governmental hospitals, the needs and concerns are similar yet vary in degrees as observed in my master's thesis conducted at the three major governmental hospitals in Egypt.

My thesis indicates that findings in the Western countries are relevant also for Egypt. The Western literature has emphasised and repeatedly acknowledged the integral part of psychosocial issues in medicine especially in pediatric oncology, satisfactory patient–physician communication is crucial for children diagnosed with cancer and their parents. Providing information about disease, treatment and treatment progress is important for the families. Nevertheless, the way information is provided, in a thoughtful and caring way, is equally crucial in creating a mutual relationship that creates confidence towards the health care team in general and the physicians specifically. This is the core of the relationship that does not seem to be established yet in Egypt.

As my thesis indicate, the parents are indeed their own child's social reference and their attributes, approach and reactions influence the child in many ways, not the least in their thoughts, feelings and behaviors. Therefore, the focus should be on providing a holistic approach where the child, the parents, the health care professionals, and the treating physician are all involved. Though a propotional increase in survival rates has been seen in Egypt at CCHE, improvements in psychosocial matters have not followed the same progression that would entail better quality of life for the children and parents and a better future to look forward to. Apparently, from our data we can see that parenthood and childhood concerns and needs are similar across the nations with, however, clear cultural and religious modifications. The Western psychosocial research, interventions and programs are applicable in the Egyptian setting if the health care providers want to increase the parents' degree of trust in the health care system and create a healthy patient–physician relationship. Therefore, it would probably be fruitful, from this perspective to transfer knowledge from Western psychosocial programs and support. In order to optimize the present

psychosocial services to the child and parents, it is also crucial to educate the health care professionals in all aspects of psychosocial care; establishing a proper communication channel and meeting the practical and emotional needs and concerns of the sick child and his or her family. It all falls under the patient–physician relationship and all that it entails.

The material we have obtained can be used to answer other questions regarding the various clinical procedures the child goes through before and after diagnosis as well as other psychosocial data. Nevertheless, additional studies are suggested and recommended, studies such as investigating the possible predictors for non-adherence from the child’s perspective and looking at the direct financial and health consequences of that. Also, future studies may provide a perspective of the child on how he or she comprehends what the physicians say and how he or she understands the diagnosis and the disease itself as well as how it reflects on his or her relationship with the parent and peers. Future intervention studies may address the needs and concerns of the child and his or her perception of the disease and hospital stay as well as the transitional period of being at the hospital and returning to home and school. In addition, there is a need to investigate the consequences and benefits of communicating with the child about the disease, treatment, disease progression and death in a society like Egypt.

10 SUMMARY IN SWEDISH – SAMMANFATTNING PÅ SVENSKA

Bakgrund: Enligt officiell statistik dör varje år över 70 procent av de barn i Egypten som diagnostiserats med cancer. Motsvarande siffra i Sverige är cirka 20 procent. En tidigare kvalitativ studie har visat att föräldrars brist på tillit till sjukvården leder till minskad följsamhet till ordinerad behandling, vilket skulle tänkas kunna påverka dosintensitet och leda till ökad mortalitet. Vi bestämde oss för att gå vidare med en studie för att undersöka om psykosociala faktorer har betydelse för den låga överlevnaden.

Syfte: Huvudsyftet med studien var att ta fram psykoonkologisk kunskap, för att kunna skapa en bättre cancervård i Egypten. Detta gjordes genom att undersöka dels samvariationen mellan psykosociala faktorer (såsom tillit och följsamhet till behandling) och överlevnad, dels föräldrarnas inställning till sjukvården och sjukvårdspersonalen. Huvudhypotesen för studien var att föräldrars brist på tillit till sjukvården vid barnets första cytostatikabehandling har en tendens att minska dosintensiteten för de efterföljande behandlingscyklerna, och därmed barnets möjlighet att överleva.

Metod: Vi utvecklade och testade två studiespecifika enkäter som riktar sig till föräldrar med cancersjuka barn vid Egyptens (och Afrikas) största barncancersjukhus i Kairo (Children's Cancer Hospital in Egypt, CCHE) och därefter genomfördes en pilotstudie. Från februari till september 2008 samlades data in från 304 föräldrar till cancersjuka barn intagna på CCHE för sin första cytostatikabehandling. Den första enkäten delades ut före den första behandlingscykeln och den andra efter den tredje behandlingscykeln. Eftersom många av föräldrarna inte var läskunniga erbjöds stöd och hjälp på sjukhuset vid ifyllandet av enkäterna.

Resultat: Av 313 tillfrågade föräldrar besvarade 304 (97 %) den första enkäten och 281 (92 %) den andra. Studien visade en samvariation mellan sjukvårdspersonalens bemötande och föräldrarnas tillit. Föräldrarnas tillit till sjukvårdspersonalen efter barnets tredje behandlingscykel samvarierade med följande faktorer vid tiden för den första behandlingen: de fick information om sjukdomen (relativ risk (RR) 13,2; 95 % KI 7,8–22,3) och behandlingen (RR 17,2; 95 % KI 9,5–31,4), de fick möjlighet att kommunicera med barnets läkare (RR 21,3; 95 % KI 11,7–38,8), de var nöjda med det sätt som barnets läkare kommunicerade på (RR 30,6; 95 % KI 14,4–64,9), de fick sina emotionella

behov tillfredsställda (RR 22,2; 95 % KI 11,8–41,9), och barnets läkare visade omtanke vid bemötandet (RR 32,0; 95 % KI 15,2–67,7). Den starkaste prediktorn för tillit vid barnets tredje behandlingscykel, efter multivariabel modellering, var att läkaren visade omtanke om föräldrarna.

Studien visade även att mer än två tredjedelar av barnen fick behandlingsrekommendationer vid hemgång och att en tredjedel av föräldrarna till barnen rapporterade att deras barn inte följde dessa (123/181). Nästan alla föräldrar upplevde att rekommendationerna var relevanta (120/123, 98 %) men tre av fyra (76 %) hade svårt att följa dem. Barnens motstånd mot behandlingen (117/123, 95 %) och otillräcklig information (105/123, 85 %) var de två huvudprediktorerna för bristande följsamhet till behandlingsrekommendationerna. Nästan alla föräldrar rapporterade brist på tillit till behandlingen (116/121, 96 %), men hade ändå för avsikt att fullfölja behandlingen av rädsla för att barnet annars skulle dö (99/123, 81 %). Av de föräldrar vars barn följde behandlingsrekommendationerna hemma, rapporterade 12 av 58 (20 %) tillit till läkare och sjukvårdspersonal.

Vi fann även att en stor andel av föräldrarna (72 %) fick besked om cancerdiagnosen från barnets läkare. Av dessa hade 39 procent barnen med sig under samtalet. Åldern bland barnen som var med under samtalet var fördelad i grupperna 0–4 år (45 %), 5–8 år (20 %), 9–15 år (30 %) och 16–18 år (5 %). Majoriteten av läkarna talade om sjukdomen som en “tumör” ($n=292$), medan “svår sjukdom” var den näst vanligaste benämningen ($n=161$). “Malign sjukdom” ($n=31$) och “cancer” (*saratan* på arabiska) ($n=18$) användes däremot mer sällan.

Avslutningsvis kunde vi se att överlevnaden i vår studiepopulation fem år efter datainsamlingen efter första behandlingen var 58 procent ($n=176$) med ett 10-procentigt bortfall (“lost to follow-up”) där troligen några barn överlevt. Majoriteten av de avlidna barnen hade leukemi ($n=22$) men även andra cancerformer som lymfom ($n=10$), hjärntumör ($n=7$), neuroblastom ($n=5$), sarkom ($n=5$) och “andra typer av tumörer” ($n=8$) förekom. Vi kunde inte se någon korrelation mellan barn som överlevt/inte överlevt gällande olika psykosociala faktorer såsom att komma i tid till behandlingen, information given vid diagnos, föräldrarnas tillit till sjukvården, läkarna, eller behandlingen.

Lärdom: Vi kunde inte bekräfta vår huvudhypotes att föräldrarnas grad av tillit påverkar dosintensiteten och därmed också barnens möjlighet till överlevnad. Den överlevnad som vi uppmätte (58 %) är högre än de överlevnadssiffror som tidigare angivits i officiell statistik och innan verksamheten vid CCHE började. Dock bör nämnas att till vår noterade överlevnad skall adderas en osäkerhet på 10 procent då 30 barn inte har kunnat följas upp på grund av att det saknas data för dessa. Däremot tycks följsamheten till behandlingen hemma bero på graden

av föräldrarnas tillit till läkare och sjukvårdspersonal, men ingen samvariation finns mellan tillit eller följsamhet och överlevnad. Vi fann en stark samvariation mellan huruvida 1) information till föräldrar gavs eller inte samt 2) på vilket sätt information gavs före barnets första behandlingscykel och graden av tillit före barnets tredje behandlingscykel.

Brukbarhet: Våra data tyder på att föräldrar till cancersjuka barn i stor utsträckning har samma tankar, känslor och behov oberoende av var i världen de befinner sig och oberoende av tradition, kultur, utbildningsgrad och teknologisk standard. Att utbilda sjukvårdspersonalen i kommunikation och bemötande kan ses som ett första led i att förbättra tilliten bland föräldrar med cancersjuka barn och öka följsamheten till behandlingen. Den psykoonkologiska kunskap vi har tagit fram skulle kunna vara till hjälp för sjukvårdspersonal med ambitionen att skapa en bättre vård av cancersjuka barn och ett bättre bemötande av deras föräldrar i Egypten eller i andra länder med arabiska befolkningar.

ACKNOWLEDGEMENTS

This work would have never been accomplished if I were alone; therefore, I want to extend my thanks to all the people who contributed to this thesis. Particularly, I want to thank:

Gunnar Steineck, my main supervisor, for believing in my study, giving me the confidence to pursue it and introducing me to the world of epidemiology. I feel privileged to have had the opportunity to pursue my doctoral studies at the Division of Clinical Cancer Epidemiology. Thank you for challenging and teaching me and for your support and flexibility. You taught me so many fundamental issues of science and life for which I am deeply grateful.

Ulrika Kreicbergs, my co-supervisor, for your guidance, encouragement and support. Thank you for your quick answers and for many challenging discussions at the division at Stockholm. Thank you for sharing your knowledge and for revising my manuscripts so carefully and for always been easy to reach. I learned so much from you professionally and personally.

Nathalie Ylitalo Helm, my co-supervisor, for your constant encouragement and enthusiasm and for always being there. Thank you for generously sharing your writing expertise and for your careful revisions of my manuscripts as well as continuous support.

Ragnar Hultborn, thank you for encouraging me and for your constructive feedback at my half-time seminar and for being you.

Nils Conradi and **co-workers** at the Regional Cancer Center West (RCC), thank you all.

Ulrica Wilderäng, my statistical savior. Thank you for extraordinary help and great discussions about statistics and much more, and thanks for being a great colleague. Your amazing support has truly been invaluable to me especially when it was the most difficult. I appreciate you so much!

A special appreciation is extended to **Eliza Åkeson**, for your enourmous help with all kinds of practical and administrative matters and for always being there during critical times and deadlines. Things have become so much smoother since you came to the department, and also, much more fun. You have been a great asset indeed. Also, **Ann Egardt**, **Susanne Amsler-Nordin**, for your invaluable help with practical matters. **Karin Abrahamsson** I truly enjoyed our language discussions and conversations. I learned a lot from you. To **Kerstin Thalén**, thank you for guiding me through all the way and for your support and help with just about everything. Thank you!

Marcus Marin, thank you for your IT help and for being so kind and helpful.

Larry Lundgren for your help with the language editing and great conversations.

Gratitude is extended to all my wonderful and supportive colleagues at the Division of Clinical Cancer Epidemiology: **Johanna Skoogh, Anna Genell, Agnetha Sundberg, Magnus Gustavsson, Dan Lundstedt, Thordis “Disa” Thorsteindottir, Junmei Miao Jonasson, Szilard Nemes, Ann-Charlotte Waldenström, Niclas Pettersson, Carina Mannefred, Jessica Mellquist, Anneli Olofsson, Louise Ericsson, Maria Olsson and Karin Stinesen Kollberg** and a special thanks to **David Alsadius** and **Caroline Olsson** for your great seminars that inspired me and taught me a lot. Thank you my great colleagues for great discussions, for teaching me so much and for being thoughtful and encouraging.

Everybody at the Division of Clinical Cancer Epidemiology in Stockholm, **Gail Dunberger, Pernilla Larsson Omérov, Tove Bylund Grenklo, Rossana Pettersén, Alexandra Eilegård, Eleftheria Alevronta, Helena Thulin, Tommy Nyberg, Arna Hauksdottir, Helene “Lene” Lindquist** and **Karin Bergmark**, thank you for hosting me during my third year of my doctoral studies, for making me feel welcome and for all great discussions about science and life and for great laughs. I feel privileged and have so many great memories with you.

My sincerest thanks to **Nancy Peterson**, my professor at The American University in Cairo. Thank you for introducing me to the world of psycho-oncology and the world of science as well as entrusting me to pursue the research and clinical work at the National Cancer Institute. You saw the potential in me and made me develop it by your constant encouragement and clinical as well as research supervision. You instilled in me an enormous passion and strong will towards the field of psychology and in particular; psycho-oncology. Life has not been the same since then, it’s so much more rewarding!

To **Karin Zetterqvist Nelson**, my master thesis supervisor at the University of Linköping, who believed in me and my study and was a wonderful supervisor by all means. Thank you for your constructive critique, constant feedback and fabulous encouragement.

To the great physicians in Cairo at various hospitals who were sceptical to my presence at first, but then extremely encouraging, supportive and open to the integration of psychology into the field of oncology. Thank you **Dr Ehsan El Ghoneim, Dr Hala Abdel Badee Nayel, Dr Dina, Dr Heba Khafagy, Dr Amani, Dr Omar Ezzeldin, Dr Achraf Mounir, Dr Hussein Metwally, Dr Shamel Souada, Dr Wesam El Ghamry, Dr Wafaa Abdel-Hadi, Dr Claudia Morcos, Dr Doris Iskander Doris, Dr Sherife Abounaga, Dr Mohamad Nasreldin, Dr Osama Refaat, Dr Mohamad Ezzat, Dr Mohammad Elshami, Dr Manal Zamzam and Patricia Pruden**.

A special thank to **Mats Kamperin** and **Mikael Hägg** at Ineko AB, printing company for your patience, flexibility and great co-operation.

To my close friends, I breathe through you and you bring joy and laughter to my heart: **Dima Ghoshe, Sabrin Mandil, Yasmine Thabet, Gihan Gamgoum, Enas Nagy Darwish, Hoda Ibrahim, Rami Al Maddah, Ahmad Mounir, Mohammad Elshami, Maysah Eid, Mai Dwidar, Maha Eid, Mai Qabbani, Farah Mousa, Lina Almerestani, Dana Jadaan, Marwa Eid, Mais S Zuhaika, Aisha Alsafty, Rehab Ala Farid Adager, Rana Afifi, Dana Ghoshe, Elshaima Abouelkheir and Mariam**

Barakeh. Thank you for precious talks and gatherings that many times have given me the extra energy needed to finish my thesis.

To my family in my home country, Lebanon: my cousins and uncles. I miss you so sincerely and I miss Lebanon so much! It's from you I get all the determination and strength to move on despite all obstacles.

To my family in Sweden, my grandparents, aunts, uncles and cousins: **Sakina, Najem, Salma, Nora, Fouad, Jamila, Engin, Alia, Azad, Jamil, Ibrahim, Mahmoud, Dana, Nermin, Seve, Juan, Jian, Dana R and Yara**, thank you for always being there for me, for making life easy when it's most difficult and for encouraging me all the time.

My family in the US: **Saleh, Amoura, Jean, Ronny, Nadine, Danny, Fatoum and Fardous**, love, passion, success, laughter and wonderful memories from our childhood in Lebanon are the first things I think of when I think of you. You and your children mean so much to me!

To my parents **Kalil El Malla and Latifée Hasan**, your endless love, encouragement and giving are absolutely striking to me. Thank you for believing in me and for always supporting me and for always loving me. Without you, I wouldn't have been able to do what I do. You have been the rock upon which our family is built. I love you more than you will ever know.

My siblings, **Abbe, Elham, Adel and Ronja**, life is beautiful and safe with you. Thank you for always taking care of me and pampering me and putting up with my hectic life. I have been a blessed baby sister. Your constant support, encouragement, endless giving and love are just amazing! You are so precious to me, and so are your families; the most humble, thoughtful and giving **Salim Kilan** and adorable **Nevin Kalil, Sarah, Nour, Omar, Reem and Yasmin**.

My deepest thanks to my family in Egypt; my parents-in-law **Hassan Hussein and Nagwan Ali**, a piece of my heart is missing when you are so far away. Thank you for your love and support, your encouragement and your enthusiasm. I couldn't have made it in Egypt during the data collection without you. Thank you from the bottom of my heart. To my sibling-in-laws **Gina Hassan** and **Ahmad Hassan**, you are great! You are so precious to me and my children. Your children **Hazem, Lilly, Mohamad** and **Yusuf** are so precious to me and they bring so much joy and laughter to my heart. To **Marwa Wahid**, you are a great sister-in-law; I appreciate you and your family so much, **Wahid, Faten, Ahmed and Eman**. Thank you beloved family for making my stay in Egypt the most extraordinary! Thinking of you!

To my three children, who missed out on a lot of Mummy time while I sought intellectual enlightenment. The cornerstones of my life and the most giving and loving angels in my life: **Mariam, Lina** and **Hassan**. I love life with you, I feel the meaning of life in your presence and I feel alive just being with you. You are my life!

“If I have seen further it is by standing on the shoulder of giants”, this refers to you indeed, **Mostafa Hassan**, my husband, my friend, my companion, my soul, the love of

my life, my better half and the father of my children. Thank you for yesterday, today and tomorrow. I couldn't have made it without your support and encouragement and without having you near me. Thank you for believing in my work. It's been a long journey together and I look forward to many more journeys by your side. Je vous aime plus que vous ne le saurez jamais!

At last, I would like to extend my sincerest gratitude and appreciation to the parents and children who participated in my study. You are the driving force in my work, you give me so much energy and love and you have taught me so much about what really matters in life. I truly wish I could ease your pain. I promise to never give up on the dream and passion that has gotten me all the way to this thesis, by your help, that is; integrating psychosocial health in the field of medicine in Egypt and the Arab World. All my respect and love to you!

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