CHAPTER 3

Involving Patients and Next of Kin to Mitigate Adverse Events Related to Systemic Anticancer Treatment

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Abstract: Medication safety in cancer care is an inherently complex field, with a potentially high risk for adverse events. Medication harm is the most common type of adverse event in cancer patients, and is often related to both systemic anticancer treatment and other medications. New systemic anticancer treatments have improved outcomes for many cancer patients, but have also introduced a whole range of new medication-related adverse events. The aim of this chapter is to provide new knowledge on how to involve patients and next of kin to prevent unnecessary adverse events related to systemic anticancer treatment. To achieve safer cancer care we need to meet the individual needs of patients and next of kin. Essential components for preserving involvement include: creating good processes for transitions of care with medication reconciliation, structured facilitation and discharge communication; patient and next of kin education; and timely follow-up after discharge. The use of electronic patient-reported outcomes can provide personalized follow-up and feedback for patients, and give healthcare professionals the opportunity to mitigate harm before it results in a severe adverse event. This empowers patients in everyday situations, and can ensure safety for patients and their next of kin. Moreover, there is a growing realization that such feedback should co-create more sound involvement of next of kin. Creating collaborative learning arenas with multiple stakeholders, including next of kin as natural and equal partners, can contribute to more targeted real-time solutions for mitigating adverse events within cancer care.

Keywords: cancer, medication safety, next of kin, patient involvement, patient safety

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Medication safety in cancer care is an inherently complex field, with a potentially high risk for adverse events related to systemic anticancer treatments. The complexity is often caused by several compelling factors connected to the biology of the disease, high-risk systemic treatments and care processes involving many different stakeholders across service levels in the healthcare system (Bergerød, 2021; Haukland, 2020). This chapter will provide insight and discussions on patient safety in cancer care focusing on how to mitigate adverse events related to medication safety through the sound involvement of the patient and next of kin.

The aim of this chapter is to provide relevant new knowledge for patient safety researchers and healthcare professionals on how to involve patients and next of kin to prevent unnecessary adverse events related to systemic anticancer treatment. The following research question will guide this chapter: What is the role of patient and next of kin in mitigating adverse events in systemic anticancer treatment, and how can appropriate involvement improve medication safety? This chapter will add to the body of knowledge on how reliable stakeholder involvement can potentially contribute to understanding more about medication safety, and how to create and sustain safe work practices across service levels in the healthcare system (Ugalde et al., 2019).

Methodology and Research Ethics

This chapter is a synthesis of knowledge based on the findings of two PhD studies and an updated literature search (Whittemore et al., 2014). We have interpreted and summarized the results from these studies in the context of medication safety to provide new knowledge on how to operationalize the perspectives of patient and next of kin involvement, in order to inform best practice in mitigating adverse events related to systemic anticancer treatment (Bergerød, 2021; Haukland, 2020).

The chapter is based on previously published healthcare research and quality assurance work done by the authors. According to the Regional Committee for Medical and Health Research Ethics in Norway, healthcare research and quality assurance work does not require approval by the committee, compare The Health Research Act §9 and The Research Ethics Act § 4.

The Norwegian Cancer System

Norway has a nationalized healthcare system that is semi-decentralized, meaning that the central government is responsible for secondary healthcare services. The service is delivered through four regional health authorities, which own and operate 20 hospital trusts (Saunes et al., 2020). The municipalities are responsible for primary care, including nursing homes, homecare, general practitioners, casualty clinics and rehabilitation services. The Norwegian Board of Health Supervision is the independent supervisory authority in Norway. All service providers are by law responsible for providing sound professional practice and for establishing safety management systems. Documentation and follow-up of adverse events should be done internally in the healthcare organizations. It is mandatory to report the most severe adverse events to the Norwegian Board of Health Supervision and the Norwegian Healthcare Investigation Board. In 2020, more than 1,000 severe events were reported (Saunes et al., 2020).

Cancer Care in Norway

In Norway nearly 300,000 people have a cancer diagnosis, and the numbers are increasing. There are approximately 35,000 new cases per year, and patients are also living longer (Cancer Registry of Norway, 2020). A typical course for a cancer patient in Norway is to first consult their general practitioner (GP). If the patient has suspicious cancer symptoms, the GP refers the patient to the hospital in line with national guidelines and care pathways. The patient is then integrated into care pathways, and goes through a rapid schedule of essential tests and requirements for the suspected diagnosis. A multidisciplinary team along with the patient reach a decision on diagnosis and treatment options. Cancer treatment and care are in general paid for by the public sector, and the patient is followed up by the hospital and the GP. The municipalities appoint a cancer coordinator for the individual patient after diagnosis. At first glance this seems like a seamless system with an appropriate distribution of responsibility and division of work. However, the cancer patient will alternate back and forth between service levels, as well as several actors in and between hospitals and services in the municipalities during the care trajectory, causing challenges related

to care transitions and involvement (Aase et al., 2017; Aase & Waring, 2020; Bergerød & Braut et al., 2020; Saunes et al., 2020).

Patient Safety and Adverse Events

There are many definitions of patient safety. This chapter uses the well-known definition provided by Vincent: "The avoidance, prevention and amelioration of adverse outcomes or injuries stemming from the process of healthcare" (Vincent, 2010, p. 14).

This definition links patient safety to adverse outcomes or injuries, caused, for example, by medication harm. An adverse event is defined by the World Health Organization as "an injury related to medical management, in contrast to complications of disease. Medical management includes all aspects of care, including diagnosis and treatment, failure to diagnose or treat, and the systems and equipment used to deliver care. Adverse events may be preventable or non-preventable" (World Health Organization, 2005).

This means that an adverse event is not caused by the disease itself, but is rather harm inflicted in or by the process of treatment or care. This is highly relevant for the cancer care field because systemic anticancer treatment not only cures or postpones the development of the disease, but could potentially cause harmful acute or subsequent effects, such as fatigue, pain and psychological harm. The harmful side effects of anticancer treatment can perhaps be regarded as poorly managed safety, however for the cancer field this is often considered to be unavoidable, justified by the argument that the patient will be able to live longer with their cancer or be cured. These potentially harmful effects may cause challenges for how the patient copes with treatment and care, but consequences and interventions seldom integrate the next of kin perspective, in terms of involvement, to mitigate these adverse events (Barlow et al., 2021; Moghli et al., 2021).

Adverse Events in Cancer Treatment in Norway

In Norway, the Patient Safety Campaign, In Safe Hands 24-7, was launched in 2011 aiming to reduce the number of patient injuries by 25%.

This campaign has continued within a patient safety program, and is now integrated into an action plan for quality and patient safety at the national level (Norwegian Directorate of Health, 2020a). None of the program initiatives focus specifically on improving patient safety in cancer care. In general, serious adverse events in the Norwegian healthcare system continue to be a big problem, and the numbers remain stable. In 2020 adverse events occurred in 13.1% of all hospital stays in Norway (Norwegian Directorate of Health, 2021b). In comparison, hospitalized cancer patients experienced an adverse event in 24.2% of admissions.

During the last decade there have been multiple studies indicating that cancer patients experience higher rates of adverse events than the general population, with an average of nearly 40% of admissions having at least one event (Cihangir et al., 2013; Hébert et al., 2015; Lipczak et al., 2015; Lipitz-Snyderman et al., 2017; Mattsson et al., 2013). Hospitalized cancer patients have a 39% higher risk of adverse events compared to other hospitalized patients. This is not due to the cancer diagnosis itself, but is associated with older age, longer hospital stays, and surgical complications (Haukland et al., 2017). By examining deceased hospitalized patients, one finds that for cancer patients dying in hospitals, the rate of severe adverse events is as much as seven times higher than for the general population (Haukland et al., 2020). The potential risks for hospitalized cancer patients are most often related to medication harm and infection (Haukland, 2020).

Several risk analyses conducted by the Norwegian Board of Health Supervision have also found that the risk for adverse events in cancer care is high in Norway (Hannisdal et al., 2013; Haukland et al., 2017) There is also a lack of national overview relating to how large the problem is within the cancer care field (Hannisdal et al., 2013).

However, the national compensatory systems and many good quality registries provide measures for surveillance. In Norway we have a national system for patient compensation after patient injuries caused by the healthcare services. Numbers from this system show that cancer is the second largest medical area with reported cases in Norway. Common reasons for compensation reported in the cancer field are failures in treatment or diagnosis (The Norwegian System of Patient Injury

Compensation, 2020). Nevertheless, even if Norway has a mandatory reporting system for the most severe adverse events, underreporting in documentation and disclosure of adverse events in hospitals remains a problem. Studies show that only one in four adverse events causing injury or death are reported through incident reporting systems in hospitals (Smeby et al., 2015).

Measuring Adverse Events

It is no surprise that cancer patients experience treatment-related toxicities, but accurate and reliable measurements of adverse events remain a major challenge for the patient safety field (Jha & Pronovost, 2016; Shojania & Thomas, 2013). Measuring adverse events is more difficult than measuring many other healthcare processes or outcomes, because adverse events need to be understood in the context of the complex systems within which they occur.

Many methods have been developed to detect adverse events, and reporting them in oncology has evolved in response to new treatments and modalities. Patient-reported outcomes (PROs) are considered the gold standard for data collection in research. Based on this, the National Cancer Institute has also developed a patient-reported outcome assessment system (PRO-CTCAE) used to evaluate symptomatic toxicity reported by the patients themselves (Basch et al., 2014; Dueck et al., 2015). The patient-reported assessment consists of 78 symptom-related questions relevant to oncology, grading common adverse events in relation to anticancer treatment. By involving cancer patients in reporting symptoms electronically themselves at an early stage, there is a potential to mitigate harm before it develops into a severe adverse event. Implementing a follow-up with PRO-CTCAE as standard clinical practice could be part of a safety surveillance system to prevent adverse events related to systemic anticancer treatment.

Next of kin are often excluded from evaluation measures (patient surveys) in healthcare services, despite the fact that healthcare professionals describe the next of kin within the cancer field as collaborative partners in quality and safety efforts (Bergerød & Dalen, et al., 2020; Stenberg

et al., 2014; Stolz-Baskett et al., 2021).We suggest a change in the evaluation of cancer care services to include measurement from the next of kin perspective. Surveys of next of kin satisfaction with care and other experiences can be useful at the department level, and could provide meaningful information as a compass and a guide in co-creating and collaborative learning, with the next of kin as an equal and natural collaborative partner in hospital cancer care (Bergerød & Dalen, et al., 2020).

Medication Harm in Cancer Care

Medication harm is reported as the most common type of adverse event in cancer patients, and is related to both systemic anticancer treatment and other medications (Haukland et al., 2017; Lipczak et al., 2011; Schwappach & Wernli, 2010; Weingart et al., 2018). Adverse drug events related to systemic anticancer treatment are of serious concern for patient safety, and in many cases cause extra unnecessary burdens to already vulnerable cancer patients (World Health Organization, 2019a).

Figure 1 compares the number of adverse events per patient for general patients, deceased patients and deceased cancer patients at a Norwegian hospital. Deceased patients experienced significantly more adverse events than general patients, and for deceased cancer patients medication harm,

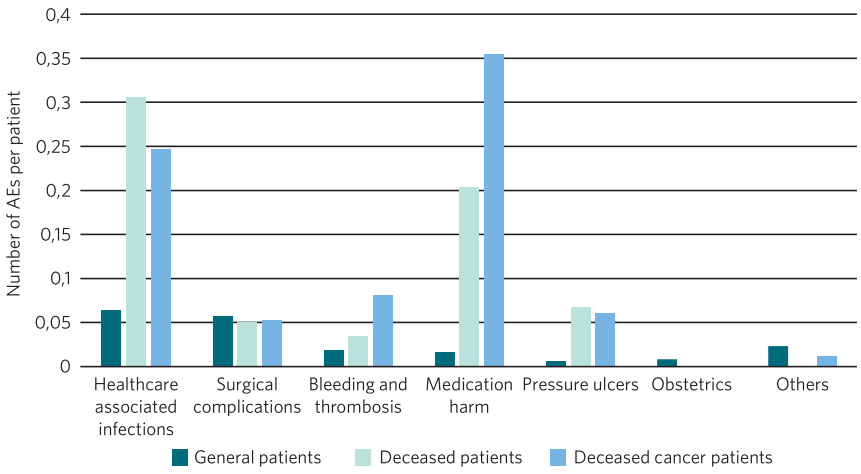

Figure 1. Comparing Types of Adverse Events Between General Patients, Deceased Patients and Deceased Cancer Patients in a Norwegian Hospital

often related to systemic anticancer treatment, such as chemotherapy and immune-checkpoint inhibitors, is by far the most common cause of adverse events (Haukland, 2020).

Chemotherapy-Related Adverse Events

Chemotherapy is classified as high-risk medication, since it has a low therapeutic index, which increases the risk of harm. Having a low therapeutic index means that the ratio of the maximally tolerable dose of the medicine to the minimal effective dose is low (Habet, 2021). In clinical practice this means that even a minimal increase in the chemotherapy dose, due to for example: drug interactions, weight changes, concomitant clinical conditions or individual variation to eliminate the medication, may cause a significant increase in effect, and potentially result in harm to the patient. For chemotherapy even doses within the recommended range often cause adverse drug reactions. Short-term toxicities such as nausea, vomiting and diarrhea are well-known adverse events related to chemotherapy treatment. For most patients, current procedures to control these are reasonably effective, preventing such side effects from developing into severe adverse events (Nurgali et al., 2018). On the other hand, neutropenia infection is a feared dose-related complication connected with chemotherapy. In the worst cases such a reaction can led to sepsis and septic shock, which is a leading cause of intensive care unit admission and mortality in cancer patients undergoing intensive cytotoxic chemotherapy (Kochanek et al., 2019). Neutropenia is itself an independent risk factor for infection. Cancer patients more often experience adverse events related to healthcare-associated infections than general patients. Chemotherapy, contributing to a reduced immune system, makes cancer patients more vulnerable to severe infections, and contributed to death in 58% of deceased cancer patients in a retrospective study from 2011–2012 (Haukland et al., 2020). The adverse events were mainly lower respiratory infections, and occurred nearly three times more frequently in cancer patients, and were the most common cause of death for cancer patients not receiving anticancer treatment during the last 30 days of life. This high incidence of hospital-acquired infections in cancer patients can be

explained by the severity of the illness, age, underlying conditions, and use of immunosuppressive medications such as chemotherapy and steroids. In addition, cancer patients often spend more time being hospitalized, contributing to a susceptibility to infections.

More than 70% of medication-related adverse events contributing to death occur in cancer patients, and most of these adverse events were related to lethal complications after chemotherapy. Patients receiving anticancer treatment during the last 30 days of life had the highest rate of medication-related adverse events, more than twice the rate of cancer patients not receiving such treatments. Anticancer treatment related adverse events contributing to death occurred only in patients who received such treatment during the last 30 days of life (Haukland, 2020). This accentuates the increased risk of severe adverse events when systemic anticancer treatment is given during the last 30 days of life, and should encourage caution when consideration providing systemic cancer treatment to patients near the end of life.

Immunotherapy-Related Adverse Events

New systemic anticancer treatments, such as targeted therapies and immunotherapy are now well-established treatments for many cancer types, and their indication for use is continuously expanding across malignancies and disease situations. The introduction of these new treatments has improved outcomes for many patients with advanced cancer. However, their introduction is also associated with a whole range of new medication-related adverse events. Unlike conventional chemotherapy, immune-checkpoint inhibitors boost the immune system and can lead to a unique constellation of inflammatory toxicities known as immune-related adverse events that are distinctly different from classic chemotherapy-related toxicities. Symptoms occur as inflammation, and can affect every organ system in the body, thus being sometimes challenging to identify. Many of the adverse events caused by targeted therapies are short-lived or reversible when therapy stops, and are often not associated with long-term adverse events (Shahrokni et al., 2016). However, if symptoms are not recognized and treated at an early stage,

immune-related adverse events can be life threatening. The rate of severe immune-related adverse events requiring immunosuppression and withdrawal of immunotherapy varies between the different immune-checkpoint inhibitors. For ipililumab (anti-CTLA-4 inhibitor), immune-related adverse events of any grade occur in up to 60% of patients, of which 10–30% are considered serious (defined as grade 3–4) (Martins et al., 2019). In comparison, anti-PD-1 inhibitors, such as nivolumab and pembrolizumab, cause severe immune-related adverse events in approximately 16% of patients (Magee et al., 2020). The combination of these two immune-checkpoint inhibitors (anti-CTLA-4 and anti-PD1) increases the incidence of severe adverse events in more than 50% of patients (Martins et al., 2019; Xing et al., 2019). Another challenge is that unlike chemotherapy-related toxicities, immune-related adverse events are not related to cumulative doses or organ reserve function, and occur more unpredictably during the course of treatment. Most often, adverse events occur during an early stage of treatment, but late-onset immune-related adverse events may also be severe. The fact that the incidence of immune-related adverse events is so high, and the outcome may be so serious and even fatal for some patients, intensifies the need for using personalized surveillance strategies that involve the patients to a greater extent.

Other Medication-Related Adverse Events

Most cancer patients are over 65 years old, and many of them often have other chronic conditions in addition to their cancer diagnosis. This adds complexity to the treatment, and is associated with polypharmacy, use of potentially inappropriate medications, and risk of adverse drug reactions. Systemic anticancer treatment potentially increases the risk of interaction with other medications and can pose a threat of increased or decreased efficacy of the cancer treatment or medication, thus causing an unintended adverse event. Thirty percent of overall cancer patients are at risk of drug-drug interactions related both to systemic anticancer treatment and supportive care treatment (Riechelmann & Girardi, 2016). Medications such as warfarin, antihypertensive medications, corticosteroids, and anticonvulsants especially have the potential for interactions

resulting in adverse events (Riechelmann & Girardi, 2016). This emphasizes the importance of medication reconciliation and close collaboration among all stakeholders involved during a course of treatment, especially the patients and their next of kin, who are often the "keepers of the story".

Narcotic agents such as opioids, sedatives and steroids are other high-risk medications often used as supportive care for many cancer patients. Patients in need of palliative care and near the end of life are also more likely to be vulnerable to medication-related adverse events. A study done in a specialist palliative care service found that 62% of the patients suffered from symptomatic adverse events (Currow et al., 2011). In palliative care the meaning of a medication-related adverse event may be considered in a broader perspective. The main fundamental goal of palliative care is the best possible symptom control with a focus on quality of life, instead of maximum prolongation of life. Not achieving these goals by, for example, omission of the administration of needed palliative medications, such as opioids, to relieve pain may also be considered an adverse event.

Mitigating Adverse Events by Involving Patients and Next of Kin

Communication and Medication Reconciliation

There is an increased availability of orally active anticancer medications that the patients administer either continuously or in periods by themselves at home. To ensure that the patient takes their anticancer medications as prescribed we need proper communication between health care personnel and patients before they leave the hospital and go home. Medication reconciliation is the formal process in which health care professionals' partner with patients and their next of kin to ensure accurate and complete medication information transfer at interfaces of care (Stolz-Baskett et al., 2021). In one randomized controlled trial, medication reconciliation decreased clinically significant medication errors by 26%. A systematic review by Herledan et al. found that medication reconciliation implemented at admission or discharge of cancer patients identified discrepancies and other medication-related problems in up to 88% and 94.7% respectively (Herledan et al., 2020).

On discharge the medication plan should always be discussed with the patient and next of kin. At the same time the patients should be made aware of the purpose of the anticancer medication they are using, the likely benefits, and potential risks. In this process patients should also be informed about possible adverse events they may expect from certain combinations, and other over-the-counter medications, food or herb interactions (e.g., grapefruit juice) that they need to avoid. These simple interventions could be the key to avoiding dangerous drug combinations.

This information should be communicated to the patient and the next of kin both orally, so that they can ask questions, and in writing so that they can consult the written information later when they get home. Communication is a two-way, relational process influenced by context, culture, words, and gestures, and it is one of the most important ways that clinicians can influence the quality of medical care that patients and their families receive (Bergerød, 2021). The format of the information provided should meet the needs of patients and next of kin while being easily understandable, with the emphasis on joint decision making. Before leaving the hospital, the patient and the next of kin need a plan for who to contact if their condition should deteriorate or if they experience side effects from the treatment generating a need for help (Nayak & George, 2021; Stolz-Baskett et al., 2021).

Personalized Follow-Up

To achieve a personalized follow-up of cancer patients and their next of kin we need to meet their individual needs, and the first step in doing so is to involve them more actively. Empirical evidence demonstrates that clinicians underreport the incidence and severity of symptoms compared to when patients themselves report how they feel (Basch et al., 2006; Lammers et al., 2019; Pakhomov et al., 2008). More importantly, most cancer patients are willing and able to self-report their own symptoms without substantial attrition. This is the case even among cancer patients with end-stage disease and poor performance status (Basch, 2010; Quinten et al., 2011).

> "It feels safe to know that my care team monitors how I am doing while at home." (Quote from a patient)

Patient-Reported Outcomes (PRO) and Outcome Measures (PROM) have shown to better describe patients' symptoms compared to reporting by health care professionals (Pakhomov et al., 2008). A recent systematic review of 22 studies including PROMs in daily cancer care found that follow-ups by PROMs had a positive effect on survival, symptoms, health-related quality of life and patient satisfaction (Graupner et al., 2021). Studies have demonstrated that electronic PROs (e-PROs) as follow-ups for cancer patients given chemotherapy treatment can reduce acute admissions to hospitals, improve quality of life and prolong overall survival by up to five months compared to standard care follow-ups (Basch et al., 2016; Jordan et al., 2018). Consequently, PROMs are seen as the preferred method and gold standard to gather information from patients in studies and in real life, as they more often give a more convincing picture of patients' wellbeing and side effects from interventions and treatments (Graupner et al., 2021).

> "It is good to sit in peace and quiet and fill in the questions when it suits me. Then it is easier to answer what I really feel." (Quote from a patient)

If cancer patients report symptoms electronically to a healthcare professional at an early stage, there is a potential to mitigate harm before it becomes severe and results in an adverse event for the patient. As the first hospital in Norway to do so, the cancer department in Nordland Hospital Trust implemented electronic patient-reported outcomes (e-PRO) follow-ups through digital monitoring as the standard of care for all patients receiving immunotherapy from June 2021, by using Kaiku Health (Kaiku Health LTD, 2020). The immunotherapy module in the Kaiku Health program is based upon the National Cancer Institute's reporting of adverse events in clinical trials of immunotherapy (Iivanainen et al., 2019). This is a web-based program for smartphones, I-pads, and home computers, and by using machine learning algorithms the software screens, grades, and alerts potential harm. Based on received treatment, each patient gets their own personalized follow-up symptom and quality

of life questionnaire sent out regularly in the software. If the patients have a high symptom burden at the start of the treatment or if the risk for adverse events is high, for example when combinations of immune-checkpoint inhibitors are given, the symptom questionnaire can be sent out every week to follow the patients closely. If the patient, on the other hand, has no symptoms the questionnaire can be sent out every second, third or even forth week, individualized to meet the specific needs of the patient. If symptoms should appear between the requested reports the patient can always fill in an extra questionnaire, measurement value or quality of life report to alert the care team of changes in his or her condition.

> "I simply feel freer, because I can fill out the form and use the app whenever and wherever I want." (Quote from a patient)

Filled-out questionnaires are submitted to the patient's care team in the cancer department, and they can see the patient's status in real time, and directly identify grades of the possible symptoms. This makes it easier to respond immediately to potentially serious immune-related adverse events and prevent further impairment of the patient, as many of the immune-related toxicities can be reversed with early intervention and use of steroids (Martins et al., 2019).

> "I was afraid it would be impersonal, but that did not happen. Now I get answers to my worries right away, if not immediately." (Quote from a patient)

At the same time as the health care professionals are alerted, the patient gets feedback on how their symptoms have evolved over time, how they should react and what they themselves can do at home to relieve the complaints. The feedback given to patients is based on international guidelines and is meant to support them in their everyday lives. Particularly mild symptoms, such as lack of appetite, feeling tired or sleeplessness, can affect quality of life for patients, but these rarely result in severe adverse events. In a busy clinical practice with limited time to talk to the patient, mild symptoms and advice on how to cope with them are often not prioritized. Providing standardized feedback to everyday symptoms encourages empowerment and safety for the patient and their family,

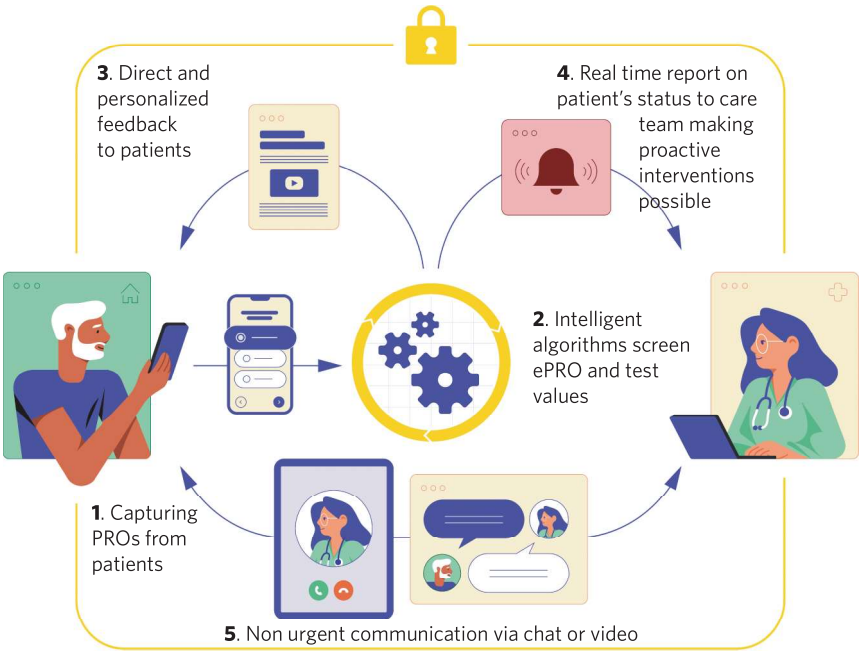

Figure 2. Illustration of How an e-PRO Follow-Up with Kaiku Health Works in Clinical Practice (Reprinted with permission from Kaiku Health)

and has proved to reduce symptoms such as pain, depression and fatigue and increase the patient's quality of life (Aapro et al., 2020). Importantly, patients are more active in their own patient journey, with more knowledge about their own symptoms and how to react to them. Figure 2 illustrates how an e-PRO follow-up with Kaiku Health works in clinical practice.

> "Like when I got a rash, I got feedback to treat it with a specific ointment. But then I got quite severe itching, and my doctor called me right away after I reported this on the app." (Quote from a patient)

The use of e-PROs can provide personalized follow-ups of patients and give healthcare professionals the opportunity to mitigate and prevent harm before it results in a severe adverse event. It could also decrease the need for emergency admissions or unplanned visits/phone calls to the outpatient clinic, which can be a burden for the patient, their family and the healthcare system (Aapro et al., 2020; Basch et al., 2016).

Knowledge about real-time follow-ups and adverse events can be clinically relevant in order to better inform patients before starting new treatments. Consequently, it may also provide information about when to end potentially harmful and high-cost anticancer treatment, as it gives healthcare personnel the opportunity to monitor and compare symptoms over time. This makes it easier to discover changes in the patient's clinical condition that might signal changing or ending a systemic anticancer treatment because of toxicities or progressive disease. For some anticancer treatments the clinical effects may occur before the response can be verified radiologically on CT or MRI scans. On radiological images we may, in such cases, see a pseudo-progression before a later response to the treatment with regression of the disease. In such cases the clinician must rely on clinical judgment, and therefore an overview of symptom development or changes in quality of life over a period are invaluable in making the right decision. If the symptom burden and quality of life of the patient have improved, this supports continuing the anticancer treatment, closely monitoring if there is a delayed radiological response.

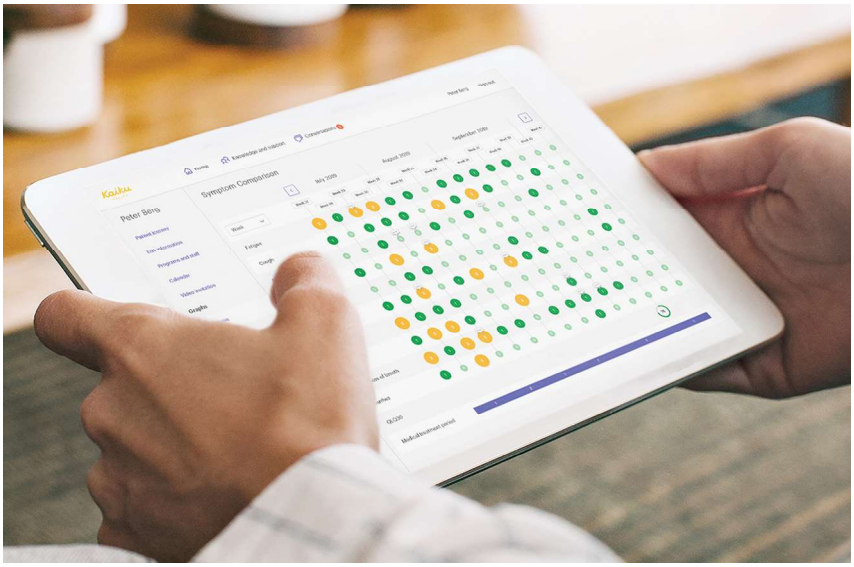

Figure 3. The Photo Illustrates How Changes in Symptoms and Values Can Be Easily Monitored Over Time Using ePRO Follow-Up (Reprinted with permission from Kaiku Health)

The Challenging Transitions

Transitions of care occur when a patient moves between facilities, sectors and staff members, for example: a transfer from the emergency room to the cancer unit; from a nursing home to a hospital; from a primary care doctor to a specialist; or from one nurse to another during a shift change. As part of their treatment cancer patients receiving systemic anticancer treatment often have numerous transitions between the outpatient clinic or cancer unit back and forth to their own home. Shifting between so many care providers and being left to yourself at home can create insecurity for patients and their next of kin. Such transitions of care increase the chances of communication errors, which can lead to serious medication harm (Aase et al., 2017; Aase & Waring, 2020).

Essential components in making the transition process safer include: medication reconciliation, structured facilitation and discharge communication, patient and next of kin education, and timely follow-up after discharge. All of these processes are unique to each cancer patient and their family and may change over time, so they need to be actively and consistently involved on all occasions. It is important to recognize that healthcare personnel always have the responsibility to facilitate the transition of care and provide safe care regardless of the service level in the healthcare system.

For post-discharge communication through new technologies, such as smartphones and applications, provide new opportunities to follow the patients closer when at home. A systematic review of studies using various technologies concluded that these technology-based interventions did not compromise safety or patient satisfaction when they measured symptoms, quality of life or psychological distress (Dickinson et al., 2014). The consequences for cancer patients in anticancer treatment can have potentially fatal outcomes in cases of missing responses to changes in the patient's condition (e.g., sepsis, bleeding). The next of kin's ability to observe the patient and to respond quickly to changes in their condition is therefore crucial, especially when the patient is between care levels. Next of kins living with the cancer patient are described as quality and safety resources, just as important as professional actors, and thus have a key role in safe transitions across care levels. Nevertheless, proper next of kin involvement is often lacking:

> "As a next of kin, you really get little information that is aimed at you on how to help and ease the treatment even if a lot happens at home." (Quote from a next of kin)

Healthcare service is a public responsibility in the Norwegian welfare state, and the formal expectations for next of kin participation are low. There are, nevertheless, strong indications that healthcare services do depend on support from next of kin to ensure high quality care for the patients (Bergerød & Braut, et al., 2020; Norwegian Ministry of Health and Care Services, 2020a; O'Hara et al., 2019). Healthcare professionals within cancer care in hospitals report that they depend on support from the next of kin to provide care quality and safety in the cancer field in hospitals. The next of kin role is often referred to as a "key piece of the puzzle", as a resource to cope with tasks they are unable to cope with because of internal (e.g., inadequate staffing, deteriorating patients) or external factors (e.g., culture, demands, economy) (Bergerød & Braut, et al., 2020).

> They often help to transport the patient, follow the patient to take blood samples, check the medicine list, and also ensure that the patient takes the medication at the right time, especially if the patient doesn't want homecare. They inject medication, measure temperature, and contact the hospital if the patient is experiencing fever. They have a huge sense of responsibility to the patient and are resource persons for the patient, us (hospital) and the municipalities. (Quote from a nurse)

Currently no recommendations exist on how to make safe transitions from hospitals to home for cancer patients or their next of kin. However, the Norwegian Directorate of Health is working on a care package process ensuring predictability for patients and their families, both in the specialist health service and in the municipal health and care services (Norwegian Directorate of Health, 2021c). Involvement is therefore crucial to strengthen the goal of creating an alliance between the family of the patient, healthcare services and voluntary organizations (Norwegian Ministry of Health and Care Services, 2020a). Next of kin involvement is more prominent than ever, and in 2021 the Norwegian government launched the first national strategy on next of kin involvement. The strategy is a clear acknowledgement of the next of kin role as a valuable societal and care contributor. The strategy has three overarching goals: 1) to acknowledge the next of kin role

as a resource; 2) attention and support so that next of kin can live good lives and combine the role of next of kin with education and work; 3) no child should have to take care of their family or others (Norwegian Ministry of Health and Care Services, 2020b). This strategy strives to have sound next of kin involvement, however there is also a long way to go before we reach these goals. Even if strategies, plans and sound involvement measures are slowly appearing, there is a great potential for translating these into clinical practice with a multi-stakeholder approach (Petkovic et al., 2020).

The development of the next of kin involvement guide for hospitals constitutes a good and promising tool (Figure 4) in terms of multiple

Figure 4. The Next of Kin Involvement Guide for Hospitals Adapted from Bergerød & Braut et al. 2021

stakeholders' engagement and sound involvement measures (Bergerød & Braut et al. 2021). The guide is built through a collective sharing of the experiences of 20 stakeholders including hospitals, healthcare professionals (nurses/doctors), patients and next of kin representatives, and researchers. The nominal group consensus method utilized in the development of the guide promoted a collaborative learning arena that resulted in mutual consensus. The guide is co-created and provides a requested tool that has the potential to support managers' and healthcare professionals' systematic work on next of kin involvement in hospitals. The next of kin involvement guide can be used either as a reflective tool to create a dialogue on how it can be refined to meet the context where involvement takes place, or as a guide with practical examples of relevant next of kin involvement measures (Bergerød & Braut et al. 2021). We argue that even if the guide is developed with the specialist healthcare system in mind, it could be pilot tested for other contexts (Bergerød et al. 2022).

Summary

This chapter has demonstrated that medication safety in cancer care is complex, with a high risk of adverse events related to systemic cancer treatment. It is no surprise that cancer patients experience treatment-related toxicities, since traditional systemic treatment, such as chemotherapy, have a low therapeutic index. This means that even a minimal increase in the chemotherapy dose due to, for example: drug interactions, weight changes, or concomitant clinical conditions, may cause a significant increase in effect and potentially result in an adverse event for the patient. Due to this, adverse events related to systemic anticancer treatment will always occur to some extent, but we argue that, by sound involvement of patients and next of kin throughout the whole cancer care continuum, severe adverse events can be reduced. Essential components in making the systemic anticancer treatment process safer include: medication reconciliation; structured facilitation and discharge communication; and sound patient and next of kin involvement focusing on individual education and timely follow-ups in the challenging transitions. The goal of measuring adverse events is to provide real-time

feedback to healthcare professionals, and thereby offer hospitals state-of-the-art quality improvement and learning opportunities to prevent such events from happening. New technology and innovations create new opportunities to engage the patient more actively in their own treatment and follow them more closely when they are at home. Personalized patient follow-ups using e-PROs give healthcare personnel a better opportunity to observe patients during treatment even when they are at home, and facilitates proactive interventions so severe adverse events can be mitigated. It also improves symptoms and quality of life, empowers patients in everyday living, and provides safety for patients and their next of kin. Next of kin play an essential role within the cancer field as collaborative partners in quality and safety efforts, and should be acknowledged as equal and natural partners in the same way as patients. The development of the next of kin involvement guide for hospitals provides a promising tool in terms of multiple stakeholders' engagement and sound involvement measures relevant for healthcare professionals and mangers throughout the healthcare system.

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