Health literacy in the context of kidney transplant recipients: a multimethod study

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Summary

Background:
Health literacy (HL) involves personal and social abilities required to make decision about health, and has gained increased focus in research, policy, health promotion and the clinic during the last three decades. In the field of kidney transplantation, there is a lack of knowledge about multidimensional aspects of HL, as previous studies have mostly focused on the competences needed to read and comprehend written health information, using quantitative measures. The ways in which the kidney recipient navigates the healthcare system, finds and appraises health information, and interacts with healthcare providers are all aspects of HL that constitute a knowledge gap. Furthermore, knowledge is lacking about kidney transplant recipients' own experiences related to HL, and how different aspects of HL might change following a kidney transplantation.

Aims:
The overall aim for this thesis was to investigate multidimensional aspects of HL in different phases during the first year following a kidney transplantation.

Methods:
The thesis consists of two sub-studies: the first using a quantitative approach, consisting of papers I and II. In the second sub-study, we used a qualitative approach that resulted in paper III.

In sub-study one, we measured HL using the multidimensional Health Literacy Questionnaire (HLQ), at approximately 5 days, 8 weeks, 6 and 12 months following the transplantation. The general self-efficacy scale, the Knowledge Questionnaire for Renal Recipients and a single question concerning self-perceived health were included in sub-study one. Clinical data was obtained from the patient electronic journal. Transplant recipients were invited to the study three to five days post-transplantation. Recruitment took place from February 2016 to August 2017. During this period, 357 patients received a kidney transplant. Of these, 217 kidney recipients were invited to participate in the study, and 196 participants were included.

In paper I, we used a cross-sectional design focusing on eight weeks following the transplantation. We used multivariable linear regression and backward elimination of variables to analyze core variables associated with HL.

In paper II, we used a prospective longitudinal design and mixed models to investigate any changes in the nine HLQ domains during the first year post-transplantation. We used backward elimination of variables to identify variables associated with HL.

In sub-study two and paper III, we used a qualitative explorative design involving observations and interviews to explore experiences related to HL during the first six months post-transplantation. Analysis and data collection were inspired by constructivist grounded theory.

Results:
In paper I, we found that participants with lower self-efficacy, lower levels of transplant-related knowledge, and lower levels of general health had lower scores in several of the HLQ domains. As such, it appears that these variables describe a more vulnerable group related to HL eight weeks following the transplantation.

In paper II, we identified two main patterns of changes in the nine HLQ domains: a) domains with a steady increase throughout the first year (“engaging with health care providers (HCP),” “navigating,” and “understanding health information”); and b) domains with a positive increase at from 5 days to 8 weeks that disappeared from baseline to 6 and 12 months (“having sufficient information,” “managing health,” and “finding good health information”). “Feeling supported by HCP” also had a significant increase from baseline to 8 weeks that disappeared at 6 months. However, a significant increase reappeared at 12 months. “Social support” was the only domain with a negative development from baseline to six months and “appraisal of health information” had no significant change. Self-efficacy, transplant-related knowledge, and general health seemed to be core variables associated with HL during the first year post-transplantation.

In paper III, the results were presented through a model consisting of three phases: the trigger phase, the information phase, and the response phase. HL was presented as an active process, influenced by context and personal factors as the transplant recipients moved between and within the three phases. The study provides insight into what motivates kidney recipients to find, share, and receive information, and how a hierarchy of resources is built and used.

Conclusions:

This study adds valuable knowledge to the clinical context. Knowledge about core variables associated with each of the nine domains of the HLQ contributes additional insight about vulnerable groups in post-transplant care. The longitudinal perspective implies that six months following the transplantation might be a challenging phase with regards to social support; the ability to manage own health; and accessing and having sufficient health information. The qualitative study illuminates how transplant recipients makes decisions about using different sources of information. Personal factors like low self-esteem, accessibility and continuity of care may prevent patients from seeking information from healthcare professionals. These findings may inform future research and practice in kidney transplant care.

List of papers

Paper I
Dahl KG, Andersen MH, Urstad KH, Falk RS, Engebretsen E, Wahl AK. Identifying Core Variables Associated With Health Literacy in Kidney Transplant Recipients. Prog Transplant. 2020:1526924819893285.

Paper II
Gire Dahl K, Wahl AK, Urstad KH, Falk RS, Andersen MH. Changes in health literacy during the first year following a kidney transplantation: Using the Health Literacy Questionnaire [submitted to Patient Education and Counselling]

Paper III
Gire Dahl K, Engebretsen E, Andersen MH, Urstad KH, Wahl AK. The trigger-information-response model: Exploring health literacy during the first six months following a kidney transplantation. PloS One. 2019;14(10):e0223533.

Abbreviations

OUS	Oslo University Hospital
LNT	The National Association for Kidney Patients and Transplant Recipients
CKD	Chronic Kidney Disease
ESRD	End Stage Renal Disease
RRT	Renal Replacement Treatment
HL	Health Literacy
HLQ	Health Literacy Questionnaire
HCP	Health Care Providers
WHO	World Health Organization
GFR	Glomerular Filtration Rate
eGFR	estimated Glomerular Filtration Rate
TX	Transplantation
NNR	Norwegian Nephrology Registry
HLA	Human Leukocyte Antigen
PTDM	Post Transplant Diabetes Mellitus
REALM	Rapid Estimate of Adult Literacy in Medicine
TOFHLA	Short Test of Functional Health Literacy in Adults
NVS	Newest Vital Sign
HLS-EU-Q	the European Health Literacy Survey Questionnaire
ES	Effect Size
CGT	Constructivist Grounded Theory

1.0 Introduction

The research group that first formulated this project has worked within the field of transplantation for many years to improve the patient education and follow-up provided to kidney transplant recipients. As such, this thesis built on knowledge from earlier work. Urstad et al. developed a comprehensive and tailored patient education program that focused on increasing transplant-related knowledge and practical skills during the first 8 weeks following a kidney transplantation (1-4). This education program was implemented in the transplantation clinic in 2014 (5-7), and is now an essential part of transplant follow-up. However, living with a new organ requires complex self-care skills that also involve the ability to find and critically assess *new* information, to know what to do and where to go to handle changing and novel health conditions. Several studies have shown that knowledge in itself is not enough to change behavior or manage complex health challenges (8-10). This project was therefore designed to gain additional knowledge and explore other strategies to investigate the kidney transplant recipient's needs throughout the first year following the transplantation.

As I started on my PhD-project in June 2016, I had worked as a nurse in the transplantation clinic for about 8 years. I had experienced the implementation of the new patient education and its positive effect on patients and nurses providing the education program. However, I often wondered whether we were able to prepare the transplant recipient for life in their own context, outside the protected environment of the hospital. With this project, I had a unique opportunity to gain knowledge about the needs of the transplant recipients and explore their post-transplant phases through the construct of health literacy.

The kidney transplant recipients are highly experienced users of the health care system, and many have had chronic kidney disease (CKD) for several years. CKD involves five stages describing the progression of the disease. In the fifth and last phase, in which end stage renal disease (ESRD) is reached, there are three treatment options: dialysis, kidney transplantation or conservative and palliative treatment that will only relieve symptoms. Dialysis and kidney transplantation are known as renal replacement therapy (RRT). Several studies have shown that receiving a kidney transplant is preferable to being in dialysis, due to better health, increased survival (11), higher quality of life (11, 12), and lower long-term costs (13). However, access to a kidney transplant is limited and requires either a living or a deceased donor. Thus, a transplantation involves tension around how to take care of this very important organ, on the part of both the patient and the health care system.

A kidney transplantation does not mean complete recovery; rather, it involves moving from one chronic condition to another. To prevent a rejection of the kidney, the transplant recipients need lifelong treatment with immunosuppressive medication, and must learn how to deal with side effects, symptoms of infections, and possible rejection of the organ. To be able to live a good life and take care of their health and their transplant, the recipient needs the ability to communicate with health care providers, navigate the health care system, find and assess available information, and utilize health care services and rights. These abilities are also known as health literacy (HL). HL depends on context (10) and changes throughout life (14). However, HL also depends on how services, organizations, and systems make health information and resources available, accessible, and adapted to individuals' HL strengths and limitations (15).

Studies of HL in kidney transplant recipients indicate that HL is associated with socioeconomic status, such as education (16-19), income (18, 19), age (19-21), ethnicity (18) (21), sex (21), and civil status (18, 22). Limited HL has further been found to be associated with lower levels of knowledge (23), symptoms of depression (22), reduced kidney function (18, 22), and medication non-adherence (22, 23). These findings reveal that limited HL may represent a risk factor. Most studies have used measurements of HL that focus mainly on reading comprehension and numeracy. These are important aspects of HL, but our understanding of HL is growing, and we now know that making decisions about one's health requires a complex array of HL resources. In addition, qualitative approaches to HL are scarce and so are knowledge of how HL might change following a kidney transplantation. Therefore, this thesis will focus on a multidimensional understanding of HL, involving both a qualitative and quantitative approach to investigate HL during the first year following a kidney transplantation.

2.0 Aims of the study

The overall aim of the study was to gain knowledge about health literacy in the context of kidney transplantation. The study involved two sub-studies, using a quantitative approach in sub-study one and a qualitative approach in sub-study two. Our specific research questions in the three papers were as follows:

Sub-study one
Paper I:

1. To what extent are selected sociodemographic and clinical variables, self-reported health, transplant-related knowledge, and self-efficacy associated with different aspects of HL eight weeks after a kidney transplantation?

Paper II:

2. A) What are the patterns of change in HL during the first year following a kidney transplantation?
   B) To what extent is HL associated with selected sociodemographic and clinical variables, self-efficacy, transplant-related knowledge, and general health during the first year post-transplantation?

Sub-study two
Paper III:

3. The main objective of the study was to explore kidney transplant recipients' experiences related to finding, understanding, and using health information, and making decisions about their health during the first six months following the transplantation.

3.0 Background and theoretical framework

The next section gives an overview of kidney transplantation and the development and understanding of HL in general and in the context of kidney transplantation.

3.1 Kidney transplantation

3.1.1 The history

The first successful kidney transplantation was performed by surgeon Joseph Murray and his team in December 1954, in Boston (24). The kidney recipient was 24-year-old Richard Herrick who had developed ESRD due to glomerulonephritis. Having a chronic kidney disease and developing ESRD was fatal at this point in medical history, as hemodialysis was not available until 1960 (25). Fortunately for Richard, his identical twin brother, Ronald, agreed to donate a kidney for transplantation. This was regarded as experimental medicine, but the transplantation was a success and Richard Herrick lived with his transplanted kidney for eight years (26). According to Murray's case report from 1958, Richard even married the nurse who attended him and became a father (27). The donor, Ronald, lived for another 56 years with his remaining kidney (28). Joseph Murray was awarded the Nobel Prize in Medicine in 1980 for his pioneering work in kidney transplantation (24).

Two years after the success in Boston, the first kidney transplantation was conducted in Norway by surgeon Leif Efskind and his colleagues at Rikshospitalet (24). The patient was 58 years old and had to remove his one remaining kidney due to cancer. This time, the transplanted kidney came from a deceased donor and to prevent organ rejection the recipient was treated with total body radiation and high doses of cortisone. Unfortunately, the patient only lived for 30 days with his transplanted kidney (24). In 1963, the first successful kidney transplantation was conducted with assistance from R. E. Wilson, a transplant surgeon from Boston, who also brought with him the immunosuppressive medication, azathioprine (24). A young man was transplanted with a kidney provided by his mother (as living donor); and he lived with his transplant for 22 years (24). In 1983, Oslo University Hospital (OUS), Rikshospitalet became Norway's national transplant center, in which all solid organ transplantations has been and are conducted (24). Over the last decade, approximately 250 to 300 kidney transplantations per year have been performed here.

Finding a matching kidney donor is a complex process that depends on both immunological boundaries and blood type. In 1956, the French immunologist Jean Dausset discovered the Human Leukocyte Antigen (HLA) (24). The HLA molecules are present on almost all our cells and play the main role in initiating an organ rejection (29). Dausset's discovery revealed that better HLA-matching between donor and recipient decreased the risk of an organ rejection and thus increased the likelihood of a successful transplantation (30). Discovering the HLA system was a revolution in transplant medicine, but at the same time, it made it more challenging to find a good match for patients awaiting a kidney transplant (24, 30), especially in a small country like Norway. However, after several meetings between researchers, clinicians, and health authorities from Sweden, Denmark, and Norway, Scandiatransplant was established in June 1969. With Scandiatransplant, all patients in the Nordic region who were waiting for a new kidney, were blood-typed and HLA-typed, and registered in a joint Nordic registry (30). A mutual registry and organ exchange policy between the countries increased the possibility of finding a matching donor. Later, Finland and Iceland were included in

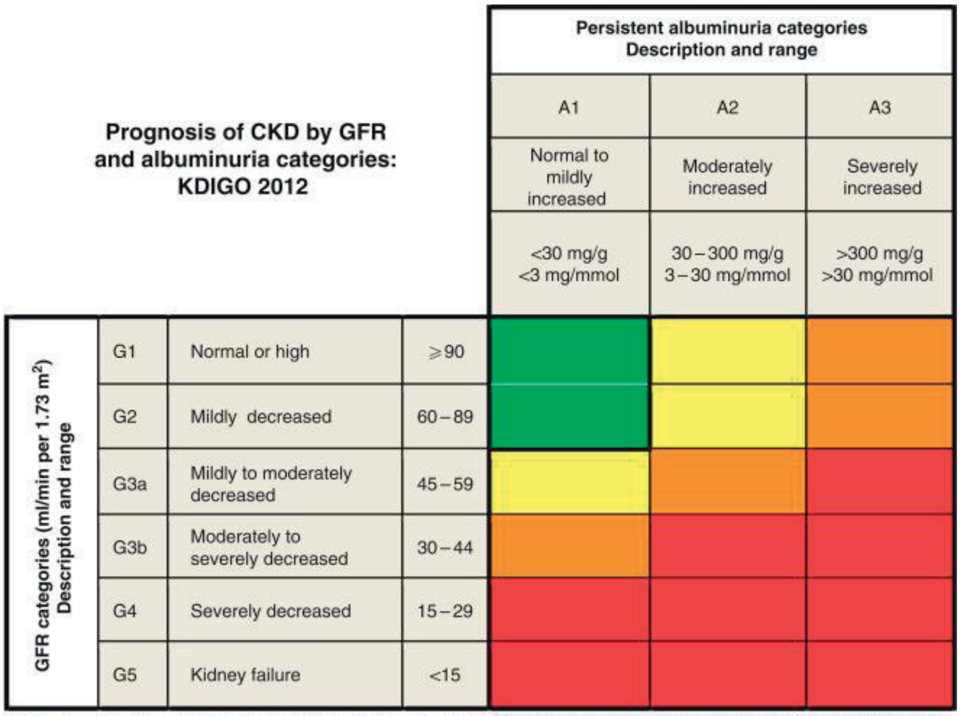
Scandiatransplant (30), and in 2017, Estonia also became an associated member. Scandiatransplant now covers a population of about 28.2 million people.

As the early phase of transplantation was considered experimental medicine, and thus the practice needed legal guidelines (24), the Norwegian government established its first act regarding transplantation in 1973, (this act was recently revised, in 2015) (31). Another important function relation kidney disease and transplantation is the Norwegian Nephrology Registry (NNR). The NNR was formally constituted in 1994 as a collaboration between the Norwegian Renal Association and OUS, Rikshospitalet. The current version of NNR represents a merging of the Norwegian Nephrology Registry and the Norwegian Renal Biopsy Registry established from 2016. All patients in Norway who develop Stage 5 CKD are included in the NNR (32).

3.1.2 Who needs a kidney transplantation?

CKD is defined by Kidney Disease Improving Global Outcomes (KDIGO) (33) as abnormalities in the kidney structure or function lasting for more than three months. As it is possible to have abnormalities in the kidney without reduced kidney function, the definition includes that the abnormalities must have health-related implications. Kidney disease may be categorized into five stages, based on cause of disease, the glomerular filtration rate (GFR), and the albuminuria category. GFR is considered to be the best index for kidney function (33), and describes the kidneys' ability to filter the urine. Figure 1 (33) describes how a GFR above 89 is classified as normal kidney function, and a GFR below 15 is classified as the fifth stage of CKD; ESRD. Albuminuria means that an increased amount of the protein albumin is detected in the urine. Usually, the glomerulus stops the leakage of protein into the urine, and increased leakage of albumin may be a symptom of damage in the kidney (34).

FIGURE 1: Reprinted with permission from KDIGO (August 2019)



Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				**Persistent albuminuria categories Description and range**		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min per 1.73 m^2) Description and range	G1	Normal or high	≥90	🟩	🟨	🟧
	G2	Mildly decreased	60–89	🟩	🟨	🟧
	G3a	Mildly to moderately decreased	45–59	🟨	🟧	🟥
	G3b	Moderately to severely decreased	30–44	🟧	🟥	🟥
	G4	Severely decreased	15–29	🟥	🟥	🟥
	G5	Kidney failure	<15	🟥	🟥	🟥

Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red, very high risk.

When reaching Stage 5 CKD with ESRD, the patient needs RRT, which may consist of either dialysis or a kidney transplantation. Patients who are not considered for, or do not wish to start RRT, will receive conservative treatment to reduce symptoms of kidney disease (33). The incidence of patients starting RRT has been stable during the last 10 years. In 2018, on December 31, 5256 patients received RRT in Norway, of whom 3624 had a transplant, 1284 were in hemodialysis, and 348 were in peritoneal dialysis. For patients starting in RRT in 2018, the main causes of CKD were vascular/hypertensive nephropathy (27%) and diabetic nephropathy (17%) (35).

There is no absolute age limit for kidney transplantation in Norway. However, there are a number of contraindications, such as malignancy during the previous year, severe comorbidity, life expectancy less than two years, active substance abuse or severe psychiatric disorders. Apart from some absolute contraindications, all Norwegian patients reaching ESRD will be evaluated for a kidney transplantation (36). The evaluation involves a thorough medical examination to evaluate whether the patient is eligible for surgery, and whether she/he would be able to follow the post-transplant medical treatment (36). If all requirements for a transplantation are met, the patient will be listed on the Scandiatransplant wait-list for a deceased donor kidney, or, if available, for a kidney from a living donor (36).

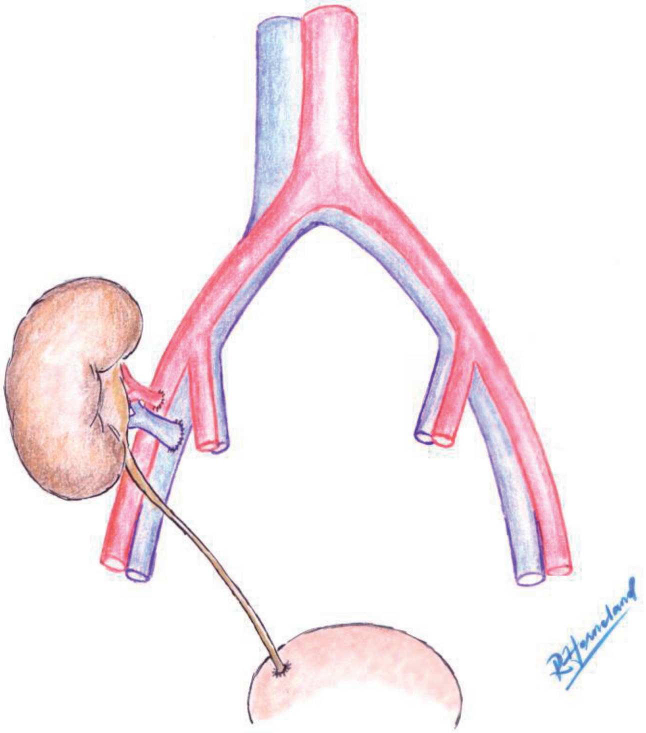
The number of kidney transplantations per year vary, and depend on the number of deceased and living donors. In 2017, a total of 274 kidney transplantations were performed (37), while the number declined to 240 in 2018 (35). Of these transplantations, between 28% to 30% came from living donors and between 16% to 13% had a re-transplant (35, 37). By the end of 2018, 337 patients were on the wait-list for a kidney transplantation (35). For the 168 recipients who received a kidney from a deceased donor, the median waiting time was 15 months, both for a first transplant and a re-transplant (35).

3.1.3 The transplantation and the postoperative phase

In Norway, there are 27 donor-hospitals with the medical equipment and health care personnel necessary to attend to a deceased organ donation. When the transplant coordinators at OUS receive a confirmation about a potential donor, the transplant surgeons agree on a matching recipient from the Scandiatransplant list. It is usually the local nephrologist who informs the recipient of the availability of the kidney. As the patient arrives at the hospital, she or he is met and informed by a nurse and a doctor and medical examinations are up-dated to ensure that there are no new contraindications. If the kidney recipient has been listed for a living donor transplantation, the donor and recipient are admitted to the transplantation ward two to three days before surgery. This is to ensure that both are fit for surgery, and that there is time for any extra examinations or treatments.

The surgical procedure for a kidney transplantation takes about four hours, including preparations, anesthesia, and waking the patient. The kidney is placed retroperitoneal (between the peritoneum and the abdominal wall) in the right or left iliac fossa. The artery and the vein of the kidney transplant are usually connected to the external iliac arteria and vein, and the ureter from the transplant is attached to the recipient's bladder (illustration 1). The location of the kidney graft is convenient, as the distance to major vessels and the bladder is short – as is the distance from the transplant to the skin, which provides easy access for ultrasounds and, if needed, biopsy (38).

Illustration 1: The artery and vein from the kidney transplant are connected to the iliac arteria and vein, and the ureter from the transplant is attached to the recipient's bladder. Printed with permission from transplant surgeon Rune Horneland.



At our center, kidney recipients are routinely transferred directly from the operating room to a high dependency unit at the surgical ward. Here, they are closely monitored for the next several hours. During the first postoperative phase, the nurses focus on symptoms of general surgical complication, and complications after a transplantation, such as obstruction of urine drainage and thrombosis of the renal artery or vein. Other associated complications that may appear after a few days are urine leakage, infections, wound dehiscence, or lymphatic fluid retention (38). Finally, yet importantly, the patients are closely monitored for possible organ rejection.

During the last three decades, the incidence of rejections has decreased significantly due to the improvement of immunosuppressive medication (39). The first sign of a possible acute rejection is usually an increase in the level of serum creatinine and secondly, the diuresis may be reduced. Upon suspicion of an organ rejection, the physician will request a biopsy of the kidney to verify this. Transplant-biopsies are classified according to Banff (40). Rejections may be categorized as follows:

- Acute T cell-mediated (cellular) rejection—typically occurs during the first three months post-transplantation (40, 41), but may happen as early as one week and as late as several years following the transplantation. A cellular rejection involves that the T-cells react on the foreign HLA antigen of the donor kidney, attack the kidney and causes acute kidney injury (42).
- Acute antibody-mediated rejection—can occur alone or at the same time as a cell-mediated rejection (41). In this case, antibodies that are specific for the donor kidney are produced by the host's B-cells (39). In some cases, an acute antibody-mediated rejection may progress into a chronic rejection, which will eventually progress into chronic kidney failure.

- Subclinical rejection is defined as an acute rejection that is diagnosed with a biopsy in the absence of clinical symptoms (39).

As part of transplant follow-up all transplant recipients at the Norwegian center undergo surveillance biopsy at six weeks post-transplantation, which is repeated after one year (36). This is done in part to exclude a possible subclinical rejection that can only be confirmed by histological changes in the kidney tissue. Whether a rejection has an impact on the long-term graft function depends on the timing of the rejection, the severity and number of acute rejections, and the degree of recovery of function after anti-rejection treatment. Generally, if the function returns to baseline, acute rejection does not necessarily cause any damage to the kidney transplant (39). The incidence of acute rejection is about 10–20%, and more than 90% of the kidney transplants function after one year (39). Acute cellular rejections seem to have less effect on the long-term graft survival than previously, likely because of early detection and effective treatment (39).

3.1.4 Medical treatment, side effects, and adherence

To prevent rejection of the transplanted kidney, the recipient depend on lifelong immunosuppressive medication, unless the kidney graft is lost and the recipient is not eligible for another transplant. The current protocol for immunosuppressive medication in Norway (in standard immunological risk recipients), consist of a daily maintenance treatment, combining three types of immunosuppressive drugs: Prednisone (Prednisolon®), Calcineurin inhibitors, Tacrolimus (Prograf®, Advagraf®, Envarsus® or Modigraf®) and Mycofenolatmofetil (Cellcept®, Myfortic®) (36). In the table below, the medications used for maintenance therapy are presented, with effects and side effects.

TABLE 1: Overview of immunosuppressive medication given as maintenance therapy after kidney transplantation.

Immunosuppressive medication	**Administration and effect**	**Side-effects**
Corticosteroids: Prednisolon®	An anti-inflammatory immunosuppressive that inhibit activations of interleukin cells that suppress T cell activation and prevent an immunologic response from the body (43). The medication is normally taken once a day after the transplantation (36).	Insomnia, mood change, hyperglycemia, increased risk of infections, dry and fragile skin, increased tendency of wounds and slower healing, skin cancer, cardiovascular diseases, osteoporosis and muscular atrophy (43, 44). Increased appetite and weight gain, Cushing's syndrome, hypertension (43, 45), increased lipid concentration, increased risk of post-transplant diabetes mellitus (45).
Calcineurin Inhibitors (CNI) Tacrolimus and Cyclosporine: Prograf®, Advagraf®, Envarsus® or Modigraf®	Calcineurin is found in the white blood cells, or the T-lymphocytes. When blocking the calcineurin, the production of pro-inflammatory cytokines is also blocked and prevent the activation and proliferation of T-lymphocytes (46). To find the right dosage of CNI, the trough levels in the blood need to be monitored closely the first weeks following the transplantation, and then regularly for as long as the patient takes the medication (36, 40). Low trough levels will increase the risk of rejection, while too high dosages may be toxic to the kidney and cause more severe side effects. CNI may be taken twice a day, with 12 hours intervals or once a day as a depot (36).	Tremor (47), diarrhea and nausea, increased risk of infections and hypertension. Lower glucose tolerance and post-transplant diabetes mellitus. Development of malignancy. Increased lipid concentrations and risk of cardiovascular disease (43, 45).
Mycofenolatmofetil: Cellcept® and Myfortic®	Inhibits the development of T and B-lymphocytes, and prevents immunological responses (48). The medication is taken twice a day with 12 hours intervals. The concentration in the blood is monitored regularly (36).	Infections, leucopenia, thrombocytopenia, diarrhea and nausea (43, 49).

The new medication regimes can be challenging for the transplant recipient, and the side effects of new medications may constitute an extra burden. To prevent some of the short and long-term side effects, the transplant recipient must often take additional medication. For example; all renal transplant recipients receive oral Bactrim® prophylactically for six months to reduce the risk of Pneumocystis infections (36). In cases where the kidney donor has been exposed to cytomegalovirus but the kidney recipient has not, the recipient will receive antiviral drugs prophylactically for six months.

Hypertension is found in most transplant recipients. This is due both to the side effects of the immunosuppressive drugs, and to the fact that kidney disease itself often leads to pre-transplant hypertension, vascular stiffness, and vascular calcification (45). Transplant recipients therefore often take two or more antihypertensive drugs (45). Research has found that hypertension is a major determinant of graft survival (50), and a focus on maintaining a normal blood pressure is thus crucial.

All patients with CKD have an increased risk of premature cardiovascular disease. After a kidney transplant, the risk decreases, when compared to remaining on dialysis. Still, some report that nearly 40% of kidney transplant recipients will experience a cardiovascular events within 36 months following the transplantation (40). Many risk factors for developing post-transplant cardiovascular disease are present prior to the transplantation and includes smoking, diabetes, obesity, hypertension, and dyslipidemia, in addition to CKD (40). On top of this, both corticosteroids and Tacrolimus increase concentrations of cholesterol, triglycerides, and lipoproteins. Most transplant recipients must therefore begin taking statins after the transplantation, to prevent the risk of myocardial infarction (45). The immunosuppressive medication may further lead to post-transplant diabetes mellitus (PTDM), which is defined as diabetes following an organ transplantation, where the diagnosis is made in a stable phase more than two months following the transplantation (51). The prevalence of PTDM is between 10–30% within the first year following the transplantation (40), and is associated with a doubling of mortality and tripling of the risk of cardiovascular events (45). A diagnosis of PTDM will also require extensive treatment and new medication for the transplant recipient.

There are several additional side effects of immunosuppressive medications that require preventive initiatives and extra attention. For example, kidney transplant recipients are at greater risk of developing certain types of cancer (40), such as skin cancer. The transplant clinical guidelines therefore recommend that the patient does monthly skin self-examination, and have an annual examination by a dermatologist (40).

The side effects of immunosuppressive medication may be overwhelming. However, the transplant recipient needs to understand the seriousness of these side effects, because they can undertake several strategies to prevent them. Exercise and a healthy diet may prevent cardiac events, the development of osteoporosis and muscular atrophy and reduce risk factors, like obesity (which may also prevent PTDM) (40, 52). Transplant recipients who smoke are strongly advised to quit, and skin cancer may be prevented by careful exposure to sun and the use of sunscreen (53). Infections may be prevented by practicing good hygiene, awareness of foods that may transmit diseases, and taking precautions when family members or visitors are sick. However, it is critical that the transplant recipient knows that although side effects may influence their quality of life, they must not stop taking their medication or change it themselves. Lee et al. (54) found that kidney transplant recipients with lower adherence also reported to have more symptoms of side effects from the medication. Good patient education, as well as the patient's insight into their own health and motivation to adhere to medication regimes and lifestyle recommendations, is therefore crucial.

Unfortunately, non-adherence is one of the biggest challenges in transplant follow-up today. Medication adherence is defined by the WHO as " 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" (55)$^{p.3}$. In the context of kidney transplant recipients, medication non-adherence is associated with early and late graft rejections and reduced graft function and graft survival (40, 44). Reduced graft function due to non-adherence may lead to decreased quality of life (56), increased health care costs (57), and reduced five-year survival rates (58). Non-adherence has been found to be the third leading cause of kidney graft losses (58), and reducing non-adherence to a minimum is therefore one of the major ambitions in kidney transplant care. A recent Norwegian study revealed that 9% of kidney transplant recipients were non-adherent to medications eight weeks post-transplantation, and that the prevalence increased to at least 32% within the first year, depending on the type of tool that was used (59). Studies investigating adherence to lifestyle recommendations and graft monitoring indicate that patients are less adherent in these areas compared to medication adherence (60, 61). The complex everyday life of the kidney transplant recipient, and the many requirements they face, underlines the importance of HL, and the importance of high-quality post-transplant care.

3.1.5 Post-transplant follow-up and patient education

During the first eight weeks following a kidney transplantation, Norwegian kidney transplant recipients are followed closely to stabilize blood levels of immunosuppressive medication, and to monitor for symptoms of infections and organ rejections, which are more common during the first six to eight weeks post-transplantation (36, 40). Usually, the transplant recipient stays at the surgical ward for one week before being transferred to the outpatient ward. Patients who live close to Rikshospitalet can then move back home, while others must stay at the patient hotel for the next seven to eight weeks. At the outpatient ward, the follow-up normally begins with three consultations per week either with a nephrologist or a transplantation-nurse. As the transplant recipient moves into a more stable phase, the number of consultations is reduced. Patients have the opportunity to travel home as often as they want during their time at the hospital, but for patients living far away, this period often involves separation from their family for some duration. After attending the post-transplant follow-up, the recipients are transferred to their local nephrologist, and after one year, they are summoned back for one last routine medical check-up and a biopsy of the kidney.

An important part of the post-transplant follow-up is the education program. Before 2014, kidney recipients received all their patient education during the first week post-transplantation, before being discharged to the outpatient ward. Between October 2007 and March 2009, Urstad et al. conducted a randomized controlled trial (RCT) to test the effect of an individual and tailored patient education program that was continued through the seven weeks at the outpatient ward (1). The education focused on three areas of transplantation-related knowledge: immunosuppressive medication, rejection of the organ, and recommendations for lifestyle. Practical skill building and interactive nursing support was also part of the intervention (1). The results of the RCT indicated that the intervention-group increased their knowledge, compliance, self-efficacy, and mental quality of life, compared to the control group, which was provided with the usual patient education (1). Due to these positive results, the education program was implemented in the clinic in 2014. As part of the education program, the recipients receive a booklet with information about life with a transplant, and their own transplant diary (62).

High-quality patient education is important following a kidney transplantation. However, studies have shown that knowledge about disease is not necessarily correlated with patient behavior (8, 63). Indeed, Kaptein et al. (8) state that self-management has been misunderstood as just another word for "education" or "giving information." Gathering information and acquiring knowledge is only a small part of managing chronic disease. The results of the Norwegian non-adherence study, mentioned above, also support these findings: although kidney transplant recipients followed a comprehensive patient education program over 8 weeks, non-adherence increased from 9% to 32% in 1 year (59). This underscores our need to have a more complex understanding of patients' behaviors and needs related to health.

3.1.6 Living with a transplant

Receiving a kidney transplant represents a transition, often described as getting life back, which is true in many ways. A meta-analysis from 2011 indicates that a kidney transplantation is associated with lower risk of death and cardiovascular events, and also higher levels of QoL, compared to remaining in dialysis (11). In 2014, Von der Lippe et al. (12) published their longitudinal study of change in self-reported QoL in Norwegian patients who transitioned from dialysis to kidney transplantation. Even though their QoL was generally lower than in the normal population, kidney transplant recipients experienced an increase in QoL, especially in domains that were associated with the burden of kidney disease (12). Lønning et al. (64) also measured QoL in kidney transplant recipients over 65 years of age. The results were similar to Von der Lippe et al., showing an increase in QoL in the first year following the transplantation. However, the new life with a transplant brings with it a great deal of responsibility, and the ability to take care of one's own health is essential. Even though a kidney transplant is preferable to dialysis, a kidney transplant recipient is still categorized as having a chronic condition, since a transplantation requires lifelong medication and close interaction with the health care system. The transition from one chronic condition to another may cause the kidney recipient to feel as though they are living a life involving several paradoxes. On one side, the kidney transplant recipient may feel more free than a dialysis patient may feel, with better health and increased energy (65, 66). On the other side, (and sometimes at the same time), a recipient may feel more unstable (66), and still restricted by medications, side effects, changes in their health condition, medical follow-ups, and uncertainty about the future (65-67).

Jamieson et al. (65) published a systematic review of 50 qualitative studies, identifying several factors that facilitated and prevented self-management or motivations to self-manage following a kidney transplantation. One of the main findings was "the over-medicalized life" (65)$^{\text{page 472}}$. Taking care of the kidney could be all-consuming, with a constant focus on self-management, such as the timing of one's medications, being aware of contagious diseases, and constantly checking for symptoms of illness associated with kidney failure or rejection of the organ (65, 67). Some recipients described wanting to escape the patient role, not only in the context of health services, but also in social situations with friends, colleagues, and family (65, 67). The risk of organ rejection was found to be an important motivation to adhere to medication regimes; at the same time, taking the medication also served as a reminder that a rejection could happen at any time (65). Forgetting to take one's medication was found to increase the anxiety of organ rejection, and sometimes also resulted in feelings of guilt for not taking good care of their kidney. When recipients sought out advice about self-management, the information was sometimes perceived as unclear or ambiguous, and several kidney recipients reported insecurity about when and where to seek out information and help (65).

These findings are relevant when trying to understand facilitators and inhibitors for HL. In the following section, I will present the history of HL, how we understand and study HL and our current knowledge about HL in the context of kidney transplant recipients.

3.2 Health literacy

HL is a complex construct that is formed through research, social, cultural, and political processes (68), and thus, the construct has been defined in multiple ways over the past 30 years. Indeed, Malloy-Weir et al. (69) published a review in 2016 identifying 250 definitions of HL. In 1997, the WHO held the 4th International Conference on Health Promotion ("New Players for a New Era: Leading Health Promotion into the 21st Century"), in Jakarta, Indonesia. During this conference, a revision of Nutbeam's health promotion glossary from 1986 was introduced, including the definition of HL used by WHO, which remains one of the most-cited definitions of HL (70): *"Health literacy represents the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health."* While the first part of the definition is more often used, the definition continues: *"Health literacy implies the achievement of a level of knowledge, personal skills and confidence to take action to improve personal and community health by changing personal lifestyles and living conditions. Thus, health literacy means more than being able to read pamphlets and make appointments. By improving people's access to health information, and their capacity to use it effectively, health literacy is critical to empowerment"* (70)$^{\text{page 10}}$.

Throughout more than 20 years of research, HL has gained increasing attention as a central part of individuals' ability to make decisions related to health. The literature reveals that low HL is associated with poorer overall health (71, 72) and mortality risk (73), less efficient use of health services (71, 74), risky health behavior (75, 76), and increased health care costs (77). Research has also found HL to be associated with a social gradient, meaning that low HL is higher in subgroups of individuals with financial deprivation, low social status, low education, and older age (14, 72, 78-82).

An individual's level of HL depends on the context and the availability and accessibility of information and health care services. As such, there has been a growing interest in addressing the responsibility of organizations and health care systems with regards to HL. HL responsiveness describes the way in which health services make health information and support available and accessible to people with different HL strengths and limitations (83).

Today, there are several challenges concerning HL, both in relation to how we define HL and how we develop knowledge related to HL. To understand these challenges, we need to understand how the construct of HL has developed.

3.2.1 The history of health literacy

The term "health literacy" was introduced by Scott Simonds in his (1974) essay on health education and social policy (84). Simonds did not provide a clear definition of HL in 1974, and the construct did not generate much interest until several years later. In the 1980s, there was increased focus on reading and numeracy skills (i.e. literacy) among the US population (85, 86). Low reading skills or inability to read or understand numbers (i.e. illiteracy) had initially been perceived as an individual problem that could influence job opportunities or educational goals (86). However, illiteracy was now identified as a political concern, a risk to the national security (85), and even a barrier for US competitiveness internationally (86). As illiteracy was recognized as a challenge, there was also a growing interest in individuals' ability to understand health information. Several studies during the 1980s indicated that health information was written at levels that exceeded the patients' reading abilities (87). This was especially challenging for the growing population who did not speak English (86). The increasing concerns about reading limitations sparked a call to investigate the magnitude of illiteracy. However, another important challenge emerged: what did literacy or illiteracy actually mean? Because of disagreements around how to define literacy, the Department of Education was asked to agree on a comprehensive definition. This resulted in the National Literacy Act of 1991, in which literacy was defined as "an individual's ability to read, write and speak in English, and compute and solve problems at a level of proficiency necessary to function on the job and in society, to achieve one's goals, and develop one's knowledge and potential" (86)$^{\text{page 28}}$. In 1992, the National Adult Literacy Survey was conducted in the United States, and the findings indicated that between 40 and 44 million of the 191 million US adults were illiterate, and another 50 million had difficulty with higher reading and problem-solving skills (88). These findings accelerated the need both to understand the consequences for patients with low literacy, and to map patients' ability to understand health information.

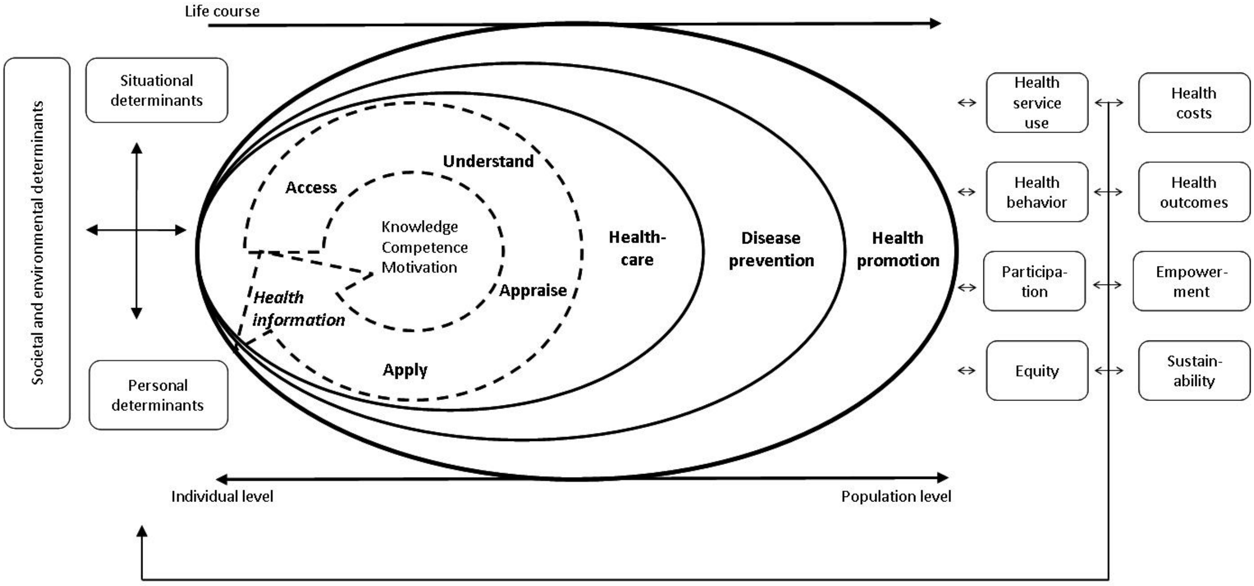
The early understanding of HL focused on the ability to understand written and verbal health information, also known as functional HL. However, HL was soon recognized as fare more complex, involving cognitive skills, such as information processing, decision-making, and problem-solving, as well as social and communicative skills (10, 89). Nutbeam (10) has defined HL as a three-part classification based on what literacy enables individuals to do:

- *Basic* or *functional literacy* involves basic reading and writing skills, so that individuals can function effectively in everyday life, and are able to read and understand the health information that they need to take care of their own health.
- *Communicative* or *interactive literacy* is more advanced. Together with social skills, this kind of literacy is important in everyday activities, including interacting with health care providers, extracting information, deriving meaning from different forms of information, and applying new information to changing circumstances.
- *Critical literacy* is the most advanced of the three types of HL and involves the cognitive skills that are required to critically analyze information. It also includes the ability to engage in shared decision-making and debates about health.

In this classification, functional literacy, or the ability to read and write, is seen as the foundation for HL, upon which a range of complementary skills can be built (90). Progression between the levels depends on cognitive development and exposure to different information, different forms of learning, and personal responses to such communication (91). Nutbeam also refers to HL as both a risk and an asset (10). In clinical care, low HL has been understood as a risk factor associated with poor health and poor adherence (92). The clinical approach to HL traditionally involved helping physicians improve their communication strategy with and guidance of patients so they would better understand and adhere to treatment regimens (93). This focus understands HL as a risk factor, or a problem that the patient and the doctor need to overcome (93). In public health, HL is seen as a personal and population asset, associated with more autonomy, control in health decisions (92), and public health promotions (93).

In 2012, Sørensen et al. (14) published an integrated conceptual model based on the review of other models of HL. The core of Sørensen's model shows the competencies needed in the process of *accessing, understanding, appraising,* and *applying* health-related information. These competencies generates knowledge and skills that enables an individual to navigate three domains of the health continuum: being a patient in the health care system, being a person at risk of disease in the prevention system, and being a healthy citizen who promotes health. Each competence represents a key element and requires cognitive abilities, like those Nutbeam describes in his classification. Following Sørensen et al.'s model, the individuals' experiences also equip them for taking responsibility and using their general and specific HL skills to make health-related decisions. Sørensen et al. describe HL as skills and competencies that develop during life. In addition, the model describes the development as a process that happens on both an individual and a population level, and that depend on the health care system and the quality of the information that is provided. Sørensen et al. (14) see HL as an asset for improving individuals' empowerment within the domains of health care, disease prevention, and health promotion (mentioned above).

FIGURE 2: The integrated model of health literacy. Used with permission from Kristine Sørensen, January 2020.



3.2.2 How do we study health literacy?

How we study HL will determine our understanding and practical use of the construct. As a response to the findings of low literacy in the 1980s and 1990s, developing ways to identify levels of literacy seemed to be a necessity. In 1991, Davis et al. published their first article on the Rapid Estimate of Adult Literacy in Medicine (REALM) (94). The test is considered to be the first measure of HL, and was developed to be a quick and practical screening tool that the physician could use to identify the patient's level of literacy. The results could be used to tailor informational material and instructions to the patient's reading levels. The REALM was designed as a reading recognition test with medical words and lay terms for body parts and illnesses, and the patient was asked to pronounce the different words. Point were allocated for the correct pronouncing of the words, and health care personnel could administer and score the test within three to five minutes (94). Four years later, in 1995, Parker et al. had developed their Test of Functional Health Literacy in Adults (TOFHLA) (95). The test focused on functional HL, defined as "the ability to use reading, writing, and computational skills at a level adequate to meet the needs of everyday life situations" (95)^{537}. The test used hospital materials like prescription labels and appointment slips, and consisted of 50 items assessing reading comprehension and 17 items assessing numerical abilities.

As the definition and understanding of HL has developed, there has been a growing divergence between how we define HL and the tools that are used to measure HL. Currently, there is no "gold standard" measure of HL, and the majority of available tools are criticized for lacking the capacity to capture the complexity involved in HL. Haun et al. (96) identified 51 instruments (26 generic, 15 disease- and-content specific, and 10 aimed at specific populations), and compared the focus of assessment with the taxonomy of skills that Sørensen et al. (14) identified through their content analysis of 17 HL definitions and 12 conceptual models (14). In addition, Haun et al. (96) included the last two skills. All together, these skills were:

- Literacy – the ability to perform basic reading tasks
- Interaction – the ability to communicate health issues
- Comprehension – the ability to derive meaning from information
- Numeracy – be able to perform basic tasks involving numbers
- Information-seeking – the ability to find relevant health information
- Application – the ability to use health information and apply information to changing circumstances
- Decision-making and critical thinking – the ability to make sound decisions about one's health and make informed choices
- Evaluation and interpretation of information
- The ability to take responsibility for one's health and health-related decisions
- Confidence to act and improve health
- Navigate the health care system

In reviewing the list of instruments provided by Haun et al. (96), most instruments covered four of these skills. Nine instruments covered only one of the skills and three tests covered nine skills at the most. Literacy and comprehension were most often the focus of the assessment, while only a few tools covered responsibility, confidence, and navigation.

Although there seems to be consensus that HL consists of more than just the ability to read or understand medical terms, the REALM and the TOFHLA are still the most used tools to measure HL (97). A review of the generic screening tools used between 2009 and 2013 found an increased use of multidimensional tools to measure HL, but several of the new screening tools were modeled after the REALM and the TOFHLA, with the addition of new item batteries. We now have a comprehensive understanding about the weaknesses of these studies, and recognize the need for developing new and better measurements (98). At the same time, the diversity of tools creates challenges, especially when trying to compare results. A study measuring HL in the Australian general population used three different screening tools and found three very different results. The proportion of participants with a less than adequate HL level was 6.8% using the TOFHLA, 10.6% using the REALM, and 26% using the Newest Vital Signs (NVS) (99).

Since 2013, more tools have been developed with a broader perspective on HL; these include a focus on individuals' ability to navigate the health care system and on social factors such as communication with health care professionals and the experience of social support in everyday life. The two multidimensional tools most relevant to mention in this context are the Health Literacy Questionnaire (HLQ) (100), and the European Health Literacy Survey Questionnaire (HLS-EU-Q) (101). The HLQ is the tool that was used to answer the research questions in this thesis (described in detail under 4.1.3.1). The HLS-EU-Q was based on the integrated model of Sørensen et al. (14). The HLS-EU-Q consists of 47 items across 12 sub-domains that integrate the following 4 cognitive domains: accessing, understanding, appraising and applying health information. The questionnaire gives one total score reflecting whether the respondent has inadequate HL, problematic HL, sufficient HL, or excellent HL. The HLS-EU-Q was used in a population survey in 8 European countries (with 8000 respondents) in 2011, and the results indicated that the proportions of the population with inadequate or problematic HL differed greatly. In Spain and Bulgaria, around 60% of the respondents answered within the two lowest categories, while in the Netherlands, less than 30% of the respondents had answers in the two lower categories. The survey showed a clear social gradient with lower levels of HL being associated with poorer health, higher use of health care services, low socioeconomic status, lower education and older age (72). However, there are some limitations with the study and the questionnaire itself; for example, the sampling strategies in the different countries led to different response rates (e.g. a 75% response rate in Bulgaria and 36% in the Netherlands). The HLS-EU-Q has also been validated in a Norwegian setting, where it was found to have certain limitations (such as ambiguous questions) (102).

A relevant discussion regarding how HL is measured concerns whether to use objective or subjective measurement. The REALM and TOFHLA are both examples of objective measures that assess functional literacy skills. The HLQ and the HLS-EU-Q are examples of self-reported and subjective measures. Both methods have their strengths and limitations. Subjective measures may be easier to manage, since assessing objective skills often requires that researchers or trained personnel administer the test. Also, a subjective measure may be associated with less stigma for the respondent, since the test asks questions concerning subjective experiences and do not involve performance on a skill-based test (97). The limitation of subjective tests, however, is the absence of information about the actual skills of the participant: although a participant might have high scores across each of the nine domains of the HLQ, we cannot make conclusions about the participant's abilities to perform practical tasks related to HL. However, when using an objective test, the skills that are tested may not be relevant to the skills that a patient actually needs: for example, a participant's ability to calculate the number of calories in a serving of ice cream (as in the NVS) gives no actual information about the skills needed following a kidney transplantation. What measurements to choose thus depends on the study's aim and the resources available. To measure the comprehension of medical information, an objective measure would likely be the best choice, while a subjective measure would provide more information about how the patient experiences the quality of the health care system (103).

There has been a significant increase in the number of screening tools available, both for generic and specialized purposes. The Health Literacy Tool Shed website (104) provides an overview of HL measurements, and contained 134 tools in August 2017 and 191 tools in August 2019. While some might argue that this is too many, we do need a range of tools to be able to investigate HL in different populations, with different ages and at different stages in life, even if the content of HL remains constant (91). Assessing HL in a healthy population or among adolescents requires different questions than when assessing HL in those with chronic disease. We also need more specific tools for specific populations, tailored to specific cultures and to individuals with specific health issues. Different tools enable more sophisticated analysis of the determinants and consequences of limitations related to HL, and provide a basis for the evaluation of interventions to improve HL (105).

The use of HL tools, regardless of their quality of complexity, will always provide limited insight into the phenomena as it plays out in real life. The majority of research in the field of HL has been quantitative, but the qualitative studies that have been conducted offer important knowledge about HL, answering questions about how patients conceptualize HL (106) and how HL may evolve through chronic disease (107) or social contexts (108). Qualitative methods have been used to validate questionnaires like the HLQ, by investigating what patients' and clinicians' HLQ scores actually mean (109). Easton et al. (110) conducted a qualitative study to investigate the stigma of low literacy, and found that patients were able to successfully conceal their low literacy by avoiding engagement with health care professionals, or by indicating that they understood the information when they did not. These are examples of the kind of knowledge that is key in the continuous work to improve health services and increase HL responsiveness. A qualitative approach is thus essential, as it allows for in-depth exploration of what HL actually involves in different contexts and for different individuals, from patient and citizens to caretakers and health care personnel.

Compared to countries like the United States and Australia, HL is rather new in the Nordic countries. Ringsberg et al. (111) conducted a review of the Nordic literature on HL published up to December 2015; this constituted 43 articles all together. The first two articles were written in 2008 – one of these was from Finland, the other from Sweden.

In May 2019, the Norwegian Ministry of Health and Care Services published their strategy to increase HL in the Norwegian population (112). The strategy involved the agreement on the Norwegian translation of health literacy, *"helsekompetanse,"* which was reached as a result of discussions in academic circles in cooperation with the Norwegian language council (Språkrådet). This strategy is an important contribution to Norwegian initiatives concerning HL, but there is still extensive work to be done in the context of HL.

Ringsberg et al. (111) raise some concerns for the future regarding HL in the Nordic countries, and one of the first centers on the conceptualization of HL. How we choose to define HL will have profound impact on the health care system and its users. It is important that we do not focus on HL as a normative scale, putting patients into high or low, correct of incorrect HL. This also involves being aware of the danger of victim blaming, where the patient is held responsible for low levels of HL and poor health. HL as a meaningful construct should therefor focus on how health care can meet the needs of a patient, based not only on their limitations but also their strengths regarding HL (111).

3.3 Health literacy in the context of kidney transplant recipients

To obtain a proper overview of the literature on HL in kidney transplant recipients, we conducted a literature review using CINAHL, Scopus, PubMed, and Google Scholar. The following words were used in the search, in different combinations: health literacy AND kidney/renal, transplant/transplantation/recipient. In addition, all relevant reference lists were searched for additional literature.

Most studies of HL in the population with CKD focus on patients prior to transplantation; however, we did find 20 articles on HL that involved kidney transplant recipients. As far as we know, there were no studies with an exclusively qualitative approach. We found 16 studies that assessed HL using 13 different HL measurements (see table 2). Only one study used a multidimensional tool (22). Three tools were developed or modified for patients with ESRD in different phases: preemptive, dialysis or post-transplant. Two studies involved interventions and four were review articles.

Based on the literature, it may seem like levels of HL may predict access to transplantation. Taylor et al. (113) conducted a large multi-center study in the United Kingdom, in which they followed 2274 dialysis patients between December 2011 and September 2013; the authors found that lower levels of HL were associated with a reduced likelihood of being listed for or receiving a transplant, independent of patient sociodemographic or clinical variables. Several other studies have similar findings (19, 21, 114, 115). There might be several plausible explanations for these results: for example, increased comorbidity and poorer health might reduce the access to transplantation. Taylor et al. (116) propose that limited HL may have a negative impact on clinician-patient communication, and may reduce the likelihood that the patient understands the positive outcomes of a transplantation and therefore does not pursue transplantation as a treatment option. Limited HL has been associated with lower socioeconomic status, which may be a mediating factor and further reduce access to transplantation (116). In addition, -type of health-care system might influence access to transplantation, as private insurance and medication prices may reduce the chance of getting a transplant.

Though kidney transplant recipients may constitute a select group, HL limitations still represent a challenge in this context. However, these limitations are difficult to comprehend, as different studies use different tools and show different levels of HL. Taylor et al. (116) conducted a systematic review and found a prevalence of limited HL between 2.4–12.3%, while Robinson et al. (117) found that 28% of the respondents had inadequate HL, and 35% had marginal functional HL. Chisholm et al. (20) had the most worrying results, finding a prevalence of 72% with low or marginal numerical literacy among kidney transplant recipients. These divergent findings illustrate some of the challenges in the field of HL research, specifically concerning the fact that the use of different HL measurements makes it challenging to compare the results. Table 2 shows the different HL-measurement tools found in the literature on HL in the context of kidney transplant recipients.

TABLE 2: Describe HLQ measurements used in the context of kidney transplant recipients.

Health literacy tools	**Describing the tool**	**References**
Rapid Estimate of Adult Literacy in Medicine **REALM**	A reading recognition test containing 66 words, measuring the ability to pronounce medical words and lay terms for body parts and illnesses.	(118) (115) (23)
Rapid Estimate of Adult Literacy in Medicine - Transplantation **REALM-T**	A modified version of the original REALM used to assess HL in the kidney transplant population. The test contains 69 transplant-related words.	(18) (21) (114)
Rapid Estimate Of Adult Literacy–Teen Version **REALM-Teen**	A word recognition test (not a reading recognition test). Adolescents are asked to pronounce 66 health words	(119)
Short Test of Functional Health Literacy in Adults **STOFHLA**	Short version of the Test of Functional Health Literacy in Adults (TOFHLA). The test use hospital material and consists of 36 items for reading comprehension and numerical abilities.	(18, 19, 117, 120)
Numeracy test based on the numeracy part in the TOFHLA	Measuring patient's ability to understand and act on numerical directions given by health care providers or pharmacist.	(20)
Newest Vital Sign **NVS**	The test involves a nutrition label from an ice-cream box, with six related questions for the respondent to answer. Four questions involving numeracy and two questions focus on reading comprehension.	(17) (121)
Newest Vital Sign **NVS** modified	Consist of two prescription labels instead of the ice cream label: one for amoxicillin and one for fluocinolone acetonide, with related questions for each label.	(114) (21)
The Decision-Making Capacity Assessment Tool **DMCAT**	Consist of seven questions relevant for the ESRD patient. The survey administrator read aloud a scenario about a patient with symptoms of chronic kidney disease, and the respondent need to decide about what to do.	(21) (114)
Short Literacy Survey **SLS**	Involve three self-reported questions: (1) *How often do you have someone help you read hospital materials?* (2) *How confident are you filling out medical forms by yourself?* (3) *How often do you have problems learning about your medical condition because of difficulty understanding written information?*	(16)
The Single Item Literacy Screener scale **SILS**	Adapted version of the SLS, with one question: *How often do you need to have someone help you when you read instructions, pamphlets, or other written material from your doctor or pharmacy?*	(113)
The Health Literacy Questionnaire **HLQ**	Measure HL in nine independent domains (described under 4.1.3.1)	(22)
Brief Health Literacy Screen **BHLS**	Consist of three questions: (1) *How confident are you filling out medical forms by yourself?* (2) *How often do you have someone help you read hospital materials?* And (3) *How often do you have problems learning about your medical condition because of difficulty understanding written information?*	(122)
Math test	Health related math abilities. The testes consisted of four basic calculations.	(118) (115)

Different measures of HL have been used to investigate a variety of variables associated with HL. Similar to other studies, limited HL has been found to be associated with socioeconomic variables such as less education (16-19), higher age (19-21), low income (18, 19), living alone (18, 22, 114), being male (21), non-white (18), and African American (21). Limited HL has further been associated with transplant outcomes like higher creatinine levels (18, 22) and lower eGFR (22), early graft failure or rejections within the first six months following the transplantation (115).

Other variables had also been investigated and studies have found low levels of HL to be associated with lower treatment knowledge (23), and immunosuppressive medication non-adherence (22, 23). Furthermore, Serper et al. (121) found that more than twice as many liver and kidney transplant recipients with limited HL reported medication trade-offs, meaning that they chose to spend money on other expenses over medication. In addition, Demian et al. (22) found that higher level of depressive symptoms were associated with lower scores across the nine domains of the HLQ. The table on the next pages provides an overview of the studies addressing HL in kidney transplant recipients.

TABLE 3: gives an overview of studies addressing HL in kidney transplant recipients.

Studies	**Tool**	**Design and sample**	**Aim**	**Findings**
Chandra et al., 2019 (119)	REALM-Teen	pre-post quasi-experimental design: 16 adolescent and young adult kidney transplant recipients	facilitate functional HL with a modified "Teach Back" method	Nine participants had REALM- Teen-scores consistent with their grade level and 7 had below grade level. Twelve of 16 patients improved their overall medication knowledge.
Chisholm et al., 2007 (20)	TOFHLA	Cross-sectional design: 36 transplant recipients	Identify numeracy literacy and associated factors.	72% were in the low or marginal numerical literacy range. Older age was associated with lower numeracy literacy.
Dageforde et al., 2014 (16)	SLS	Retrospective study: 360 adults, consisting of 105 living kidney donors, 152 kidney transplant recipients with kidney from deceased donor, 103 and living donors.	evaluated the associations of patient and demographic characteristics with HL in living kidney donors, living donor kidney transplant recipients, and deceased donor recipients	Limited HL was found in 49%, while 41% had moderate and 10% had low HL. Living donors had the lowest prevalence of low HL (6%), or moderate HL (34%). Deceased donor recipients had the highest prevalence of low (14%), or moderate HL (46%).
Demian et al., 2016 (22)	(HLQ	Cross-sectional design: 96 transplant recipients, at least 6 months post-transplant.	Investigating the effect of lower HL on medication adherence	Non-perfect adherence was reported in 75%. Non-adherence was associated with lower scores in six of nine HLQ-domains. A higher level of depressive symptoms was associated with lower scores in all domains of the HLQ.
Escobedo et al., 2013 (17)	NVS	Cross-sectional design: 44 participants (15 in dialysis, 28 kidney transplant recipients and 1 undefined)	Identifying levels of HL in patients seen at a suburban transplant center	Thirty percent had high likelihood of limited HL and 11% had a possibility of limited HL. Fifty-nine percent had adequate HL. NVS-scores was positively associated with level of education, while having Spanish as first language was negatively associated with NVS-scores
Gordon and Wolf, 2009 (18)	REALM-T S-TOFHLA	Cross-sectional design: 124 kidney transplant recipients	Examine the relationship among kidney transplant recipients' health literacy levels, transplant knowledge, and graft function	Using the S-TOFHLA, 91% had adequate HL, 4% had marginal and 5% had inadequate HL. The REALM-T was used as a measure of transplant related knowledge and 81% were unfamiliar with at least 1 kidney transplant-related term.
Kazley et al., 2014 (21)	REALM-T, NVS (modified) DMCAT	Cross-sectional design: 127 respondents: 30 patients undergoing vascular access, 36 patients in dialysis, 31 pre-transplant and 30 post-transplant participants	Testing the Decision-Making Capacity Assessment Tool (DMCAT), a new tool for assessing HL in patients with end stage renal disease (ESRD).	Scores from all the three tools indicated that patients undergoing vascular access, and dialysis had lower scores than pre and post-transplant recipients. Post-transplant recipient had the highest score in all tests. Using the NVS, 4.7% had low HL, 8.7% had marginal and 78% had adequate HL. Using the REALM-T: 18.9% had low HL, 24.4% had marginal and 53.5% had adequate HL.
Kazley et al., 2015 (114)	REALM-T NVS (modified) DMCAT	Cross-sectional design: 92 participants (30 in vascular access clinic, 31 pre-transplant, 31 post-transplant)	Assess the relationship between health literacy and transplant outcomes	Higher levels of HL in all the three tools was significantly predicting whether the participants were listed for a transplantation, and higher levels on the NVS and the DMCAT predicted whether the participants received a transplant..
McNaughton et al., 2014 (122)	Brief Health Literacy Screen (BHLS)	Cross-sectional design: 46263 and 1983 transplant recipients with different organ transplantations (according to table 1)	Evaluate the relationship between low HL and elevated blood pressure (BP)	Low HL was found in 23%. Elevated BP was more frequent among patients with low HL. Low HL was associated with extremely elevated BP and elevated BP among those without diagnosed hypertension. 1571 transplant recipients had adequate HL and 412 transplant recipients had low HL (according to table 1).
Miller-Matero et al., 2016 (115)	REALM Health-related math test	Longitudinal prospective design: 398 patients considered for different transplantations, 95 were considered for a kidney transplant (no information about how many was transplanted in the study period)	Investigate whether health literacy and cognitive impairment were related to listing for transplant and post-transplant outcomes.	Patients with low score on the REALM were less likely to be listed for transplantation and more likely to be removed from the list and miss pre-transplant appointments, experience early graft failure or rejections within the first six months following the transplantation. Patients with limited math abilities were less likely to be listed for and receive a transplant, and more likely to be readmitted to hospital within the first six months following the transplantation.
Patzer et al., 2016 (23)	REALM	Longitudinal design: 99 kidney transplant recipients (including 7	Evaluate the prevalence of medication understanding and non-adherence of drug	Limited HL was found in 24.7%.. Fewer months since transplantation and limited HL were associated with higher odds of medication non-adherence.

		kidney -and pancreas recipients)	regimens among kidney transplantation recipients and examine associations with clinical outcomes.	
Robinson et al., 2015 (117)	S-TOFHLA.	Randomized controlled trial: 170 kidney transplant recipients with different ethnic backgrounds (62 non-Hispanic white, 60 non-Hispanic black, and 48 Hispanic/Latino).	Evaluated the impact of a culturally sensitive sun-protection program on knowledge, intentions to use, and use of sun protection before and 2 weeks after education	28% had inadequate HL and 35% had marginal functional HL. Hispanic/Latino participants with initially inadequate HL increased their knowledge more than non-Hispanic white and black participants with adequate HL.
Serper et al., 2018 (121)	NVS	Prospective design: 201 transplanted recipients: 103 liver transplant recipients 98 kidney transplant recipients	Evaluated the association of "medication trade-offs"—choosing to spend money on other expenses over medications—with medication non-adherence and transplant outcomes	17% of patients reported medication trade-offs and more than twice as many transplant recipients with limited HL reported medication trade-offs. Limited health literacy and ≥3 comorbid conditions were associated with trade-offs. Patients with trade-offs were more likely to report non-adherence to medications.
Taylor et al., 2016 (123)	SILS	Cross-sectional design: 6842 patients: 2621 incident dialysis, 1959 wait-listed, 2262 incident transplant.	Investigated the prevalence and associations of limited HL with access to transplantation and transplant Outcome measures	Limited HL was found in 20% of dialysis patients, in 15% of wait-listed patients and in 12% of transplant recipients. HL was positively associated with transplant wait-list, preemptive transplantation, and getting a kidney from living donor.
Taylor et al., 2019 (113)	SILS	Prospective design: 2274 patients from 72 different kidney units in the UK	Investigating the relationship between limited health literacy and clinical outcomes and access to kidney transplantation.	Lower levels of HL was associated with reduced likelihood of being listed for a deceased-donor transplant, receiving a living-donor transplant, or receiving a transplant from any type of donor, independent of patient sociodemographic or clinical variables.
Weng et al, 2013 (120)	STHOFLA	Cross-sectional design: 252 kidney transplant recipients. 62.7% had a kidney from living donor.	Determine the prevalence and correlates of medication non-adherence among kidney transplant recipients	The majority of participants had excellent adherence and 97.7% had adequate HL. HL was not found to be associated with non-adherence to immunosuppressive medication.
Review studies	**Relevant studies included in the review:**		**Aim**	**Findings**
Dageforde et al., 2013 (124)	Gordon and Wolf, 2009 (18) Escobedo et al., 2013 (17) Chisholm et al., 2007 (20)		Define HL and describe available assessment measures in patients with CKD, ESRD and kidney transplant recipients.	Summarize findings in each study in accordance with existing summary in the present table.
Fraser et al., 2012 (125)	Gordon and Wolf, 2009 (18)		Measure the prevalence of limited HL in patients with CKD and associations with associated variables	Limited HL is common in CKD-patients with a pooled prevalence of 23%. Limited HL was associated with low education, low income, lover levels of kidney disease knowledge, lower likelihood of being referred for transplantation and higher mortality.
Jain and Green, 2016 (126)	Dageforde et al., 2013 (124) Dageforde., 2014 (16) Gordon and Wolf, 2009 (18) Kazley et al., 2015 (114) Escobedo et al., 2013 (17)		Present current tools to measure HL in patients with CKD	REALM is the most used measure of HL, followed by the TOFHLA and the short version STOFHLA. BHLS. NVS.
Taylor et al., 2017 (116)	Gordon and Wolf, 2009 (18) Kazley et al., 2014 (21) Weng et al., 2013 (120)		Summarize the evidence for associations between reduced HL and patient outcomes in CKD	Pooled prevalence of limited HL was 25% in CKD patients not in dialysis, 27% in patients with dialysis and 14% in kidney transplant recipients. Summarize findings in accordance with existing summary in the present table.

There are several challenges when assessing the different studies of HL in the context of kidney transplantation. The first one is the use of different tools, which makes the results more difficult to compare. Second, most of the studies measured functional HL and add little knowledge about how the kidney transplant recipient navigates the health care system, assesses health information, or communicates with health care providers. Third, the samples are often small, such as Chisholm et al.'s study of 36 participants (20) or Escobedo et al.'s study of 44 participants (only 28 of whom had received a kidney transplant) (17). Thus, while studies have given us important information about HL in the context of kidney transplant recipients, they also create a knowledge gap. Primarily, we need more knowledge about the multidimensional aspects of HL, and thus more studies involving a qualitative approach. In addition, previous studies have largely been cross-sectional; as such, we need more knowledge about how HL might change following a transplantation.

4.0 Materials and methods

In the next section, I will place the study within a scientific context and present the methods used in the two sub-studies of the thesis.

The present thesis is placed within the pragmatic research paradigm. Pragmatism involve that the world and reality is not static but "in a constant state of becoming" (127)$^{p.3}$, and that reality can never be absolute, but relates to our experiences (127). Within this perspective, our knowledge and reality are socially constructed (127). As such, HL is understood in light of social processes, through the way we talk about it, how we study HL, and how we use HL in clinical practice and in political contexts. Consequently, the construction of HL will always be in progress.

Using pragmatism as a research paradigm, involves making methodological choices based the best way to answer the research question (127, 128). Hence, to be able to illuminate the complexity of HL in the context of kidney transplantation, we chose to use both quantitative and qualitative approaches. The mixing of the two paradigms within the field of research is described as mixed methods or multiple methods. According to Tashakkori et al., (129) mixed or multiple methods is an eclectic and pragmatic approach to employ useful combinations of tools and methods to answer multifaceted questions. Mixed methods are not easily defined, as there are several definitions and opinions on the subject, especially regarding the conceptualization of the actual mixing (129) – for example, a frequent debate concern where in the research process the mixing should occur. Nevertheless, there seems to be agreement that the results should involve the mixing of both methods (130). In our study, we conducted parallel data collection, but analysis was done sequentially, and the results were presented as two quantitative papers and one qualitative paper. Since the results were not presented together, we define our study as a multiple methods rather than a mixed methods study.

4.1 Sub-study one: Identifying levels and changes in health literacy and associated variables (papers I and II)

4.1.1 Design

In sub-study one, our objective was to investigate levels of HLQ scores and identify variables associated with the HLQ domains. Furthermore, we aimed to investigate whether HLQ scores changed throughout the first year following the transplantation. We used a quantitative design and patient-reported outcomes were measured at 5 days (T1), 8 weeks (T2), 6 months (T3) and 12 months (T4) post-transplantation. These time points were chosen as they could reflect important phases following the transplantation. At eight weeks, the transplant recipients were transferred back to their home context and local follow-up. At six months, the recipients had new experiences with every-day-life, involving adjustments and possible challenges relevant to HL. Twelve months represented a long-term perspective, as the recipients were in a more stable phase.

In paper I, we used a cross-sectional design to identify levels of HL eight weeks post-transplantation (T2). In paper II, we used a longitudinal prospective design to identify changes in HL during the first year post-transplantation, using all four time points (T1, T2, T3 and T4).

4.1.2 Study population

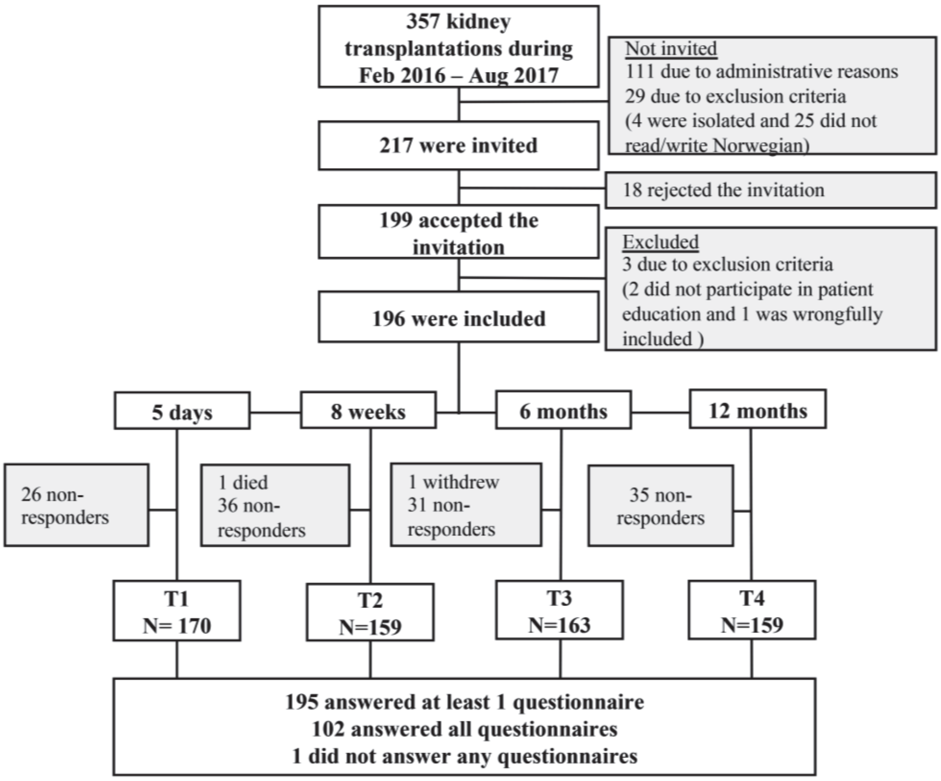
Kidney transplant recipients were invited to participate in the study between February 2016 and August 2017. Nurses trained to provide the informed consent invited potential participants within the first three to five days after the transplantation. The inclusion criteria were as follows:

- Being 18 years or older
- Being able to read and understand Norwegian well enough to answer the questionnaire
- Being able to participate in the patient education program

Since the questionnaires were distributed in paper format, we experienced practical challenges with the inclusion of patients who were isolated due to contagious diseases. Hence, we needed to exclude these patients from the study. This involved four patients.

During the inclusion period, 357 patients received a kidney transplant. One hundred and eleven patients were not invited to participate in the study due to administrative reasons. Twenty-nine patients were not invited due to exclusion criteria. Two hundred and seventeen patients were invited, of whom 199 agreed to participate. Three participants were excluded, as two did not participate in the patient education program and one had a simultaneous kidney and pancreas transplantation and was therefore wrongfully included in the study. Thus, a total of 196 participants were included in the study, comprising 55% of the patients who received a kidney during the recruitment period (figure 3).

FIGURE 3: Flowchart



In paper I, we used data gathered at 8 weeks (T2), and 159 participants answered the questionnaire. One participant died before 8 weeks, and 36 did not respond to the questionnaire. Of the 159 participants, 143 gave informed consent for the retrieval of clinical information from the electronic patient journal. For paper II, 196 participants were included and 195 participants answered the questionnaire at least once during the first year, while 102 participants answered all the questionnaires. Of the 196 participants, 178 gave informed consent for the retrieval of clinical information from the electronic patient journal.

4.1.3 Data collection and outcome measures

The first questionnaire (T1) was handed out at the surgical ward approximately five days following the transplantation. The second questionnaire (T2) was distributed at the outpatient ward during one of the last consultations with a nurse. The third questionnaire (T3) was sent by mail six months post-transplantation together with a postage-paid envelope. Participants who did not return the questionnaire received one phone call to remind them of the questionnaire. The fourth and final questionnaire (T4) was given to participants at their one-year follow-up at the outpatient ward.

Table 4 gives an overview of the outcome measures in the questionnaire and when they were collected.

TABLE 4: Outcome measures in sub-study one

Outcome measures	**Instruments**	**T1 5 days**	**T2 8 wees**	**T3 6 months**	**T4 12 months**
Demographic and clinical characteristics	Sex	X			
	Civil status	X			
	Education	X			
	Employment status	X			
	Ethnicity	X			
	History of previous transplantation	X			
	Duration of kidney disease	X			
	Type of kidney disease	X			
	History of dialysis	X			
	Donor status	X			
	Postoperative complications	X			
	Episodes of rejection			X	X
Health literacy	Health Literacy Questionnaire	X	X	X	X
General health	Single item question on self-perceived helath	X	X	X	X
Transplantation-related knowledge	Transplantation knowledge questionnaire	X	X	X	X
Self-efficacy	General perceived self-efficacy scale	X	X	X	X

4.1.3.1 The Health Literacy Questionnaire (HLQ)

The Health Literacy Questionnaire (HLQ) was developed using a validity-driven approach including workshops and interviews, psychometric analysis and cognitive interviews to develop a holistic picture of HL (100). The questionnaire contains 44 questions across 9 independent domains. The nine domains are presented under together with the short-form, used in the thesis.

1. Feeling understood and supported by the health care providers
   "Feeling supported by HCP"
2. Having sufficient information to manage my health
   "Having sufficient information"
3. Actively managing my health
   "Managing health"
4. Social support for health
   "Social support"
5. Appraisal of health information
   "Appraisal of health information"
6. Ability to actively engage with health care providers
   "Engaging with HCP"
7. Navigate the health care system
   "Navigate"
8. Ability to find good health information
   "Finding good health information"
9. Understanding health information well enough to know what to do
   "Understanding health information"

In the first five domains (1-5), respondents are asked "how strongly do you disagree or agree with the following statement?" followed by four or five statements and the four possible responses: “strongly disagree,” “disagree,” “agree,” or “strongly agree.” These domains mainly reflect experiences. The next four domains (6-9) center around capability: the participants are asked “how easy or difficult are the following tasks for you to do now?” with five or six items for each domain. Five possible responses are provided: “cannot do or always difficult,” “usually difficult,” “difficult,” “usually easy,” or “very easy” (100). The HLQ covers a broad range of HL dimensions that consider the capability of an individual to understand, engage with, and use health information and health services. Furthermore, the HLQ also reflect the capability of an organization to provide services that enable individuals to understand, engage with, and use health information or services (100).

The development of the HLQ was guided by Bloom’s revised taxonomy, which focuses on the cognitive domains of learning and classifies thinking according to six cognitive levels of complexity (100). The taxonomy is hierarchical, in that an individual cannot reach a higher level without mastering the lower ones. The same cognitive development is found in Nutbeam’s three levels of HL (10), which also informed the construction of the questionnaire.

The HLQ does not give a total score but, instead, nine domain-specific scores. The scores are calculated by adding each item score together and then dividing the overall score by the number of items in the domain. A higher score indicates higher HL. In the present study, the scores were conducted with the use of the HLQ scoring algorithm included in the user manual from the developers.

The translation of the HLQ was undertaken according to a standardized protocol prepared by the authors of the HLQ (131), and through cooperation with and verification by the first author of the HLQ, Richard Osborne. Moreover, the Norwegian HLQ was tested in a group of 18 participants through an online survey and a validation of the Norwegian HLQ was conducted among 368 first-year nursing students (132).

4.1.3.2 Transplant-related knowledge

The Knowledge Questionnaire for Renal Recipients (2) was developed for Norwegian kidney transplant recipients and was chosen as an outcome measure. Identifying whether knowledge was associated with different aspects of HL would be of clinical interest as it could identify vulnerable patients in the transplant follow-up phase.

The Knowledge Questionnaire for Renal Recipients (referred to as “the knowledge questionnaire”) contains 14 statements concerning the importance of medication, rejection symptoms, and lifestyle. Each statement is rated using a 5-point scale anchored from the left, with the wording “totally disagree,” “slightly disagree,” “neither agree nor disagree,” “slightly agree,” and “totally agree” (2). The correct answer for each statement is always “totally disagree” or “totally agree.” The other answers are thought to reflect uncertainty, and are not given points. The questionnaire gives a total knowledge score from 0–14, with higher scores indicating a higher level of knowledge. The questionnaire allows for two missing items, and the respondent receives a total score based on the correct number of answers provided.

The questionnaire was developed and validated in a Norwegian context (2). Originally, the questionnaire contained 19 questions. However, in a recent revision, the developers of the questionnaire excluded five questions (items 8, 9, 12, 15 and 17), since they were no longer relevant to the present patient education practice.

4.1.3.3 General self-efficacy scale

Self-efficacy is part of Banduras' social learning theory and was included in the WHO's health promotion glossary in 2006, where it is defined as *"beliefs that individuals hold about their capability to carry out action in a way that will influence the events that affect their lives"* and *"self-efficacy beliefs determine how people feel, think, motivate themselves and behave. This is demonstrated in how much effort people will expend and how long they will persist in the face of obstacles and aversive experiences"* (133)$^{p.343}$. Self-efficacy has been found to be a mediating factor in understanding health-related choices and health behavior (134). We therefore included the General Self-Efficacy Scale (GSE) (135) as an outcome measure. This questionnaire measures an individual's perception of their ability to cope with novel or challenging tasks across situations and to reflect optimistic self-belief (136).

The GSE was developed by Jerusalem and Schwarzer in 1981 and is one of the most frequently applied questionnaires measuring self-efficacy (134, 137). The questionnaire contains 10 statements and the response alternatives are "not at all true," "hardly true," "moderately true," or "exactly true." The scores for each item give a total GSE-score between 10 and 40 points and a higher score indicates higher self-efficacy (135). The questionnaire allows for three missing items and the total score is calculated by adding the scores and dividing the total by the number of items answered by the respondent.

4.1.3.4 General health

We used a single item question to assess the participants' self-perceived evaluation of their overall health. The question was posed in the following way: "In general, how would you say your health is?" The participants were then given the following responses from which to choose: "excellent," "very good," "good," "fair," and "poor." A higher score indicates a lower evaluation of health (138). The scores were reversed to make the interpretation of the analysis easier. The question has been translated and validated in Norwegian (139).

This single-item measure of self-reported health has been found to be a powerful predictor of clinical outcomes (140), and was included in the questionnaire to determine whether it could be associated with any aspects of HL.

4.1.3.5 Clinical and sociodemographic variables

Table 4 gives an overview of the clinical and sociodemographic variables collected via the questionnaires. From the electronic patient journal, we obtained information about comorbidity, postoperative complications, infections, episodes of rejections in the first 8 weeks, time in dialysis and blood test results at 8 weeks and 12 months post-transplantation. We were also able to verify information about dialysis pre transplantation, donor status, and postoperative complications.

Surgical complications were registered if the patient needed interventions, such as re-operation or drainage of fluid loculaments. Postoperative infections were registered in cases where the patient needed treatment with antibiotics. Cytomegalovirus was registered if the participants had a viral load of 600 copies/ml or more, which requires treatment with antiviral medication.

Comorbidity was calculated using the Charlson comorbidity index. While the Charlson comorbidity index includes a score for age, this was not considered relevant in the present study, since we wanted to identify the burden of having several diagnoses; comorbidity including age would have also led to collinearity with the age variable in the regression models. The participants were not given scores for kidney disease.

4.1.4 Data analysis and statistical methods

4.1.4.1 Power analysis

The present study had shared data gathering with another study, with the objective to evaluate the patient education program and patient follow-up. Due to the research questions in the overall project description, the aim was to include 200 kidney transplant recipients. Based on available data, we conducted a power analysis to assess whether we had sufficient numbers of participants to include variables of interest in the regression analysis and the mixed models.

The power analysis was calculated using Tabachnick and Fidell's statistical rule of thumb: $N \geq 50 + 8m$ (m= number of independent variables) (141). In the first paper, we started out with a maximum of 11 variables in the first model. We then needed $50 + (8 \times 11) = 138$ participants in our sample, and the sample comprised 159 participants. In the final models, there was a maximum of nine variables. In paper II, we used fewer variables, and had a higher N.

4.1.4.2 Statistical analysis

Statistical analysis was conducted with the use of IBM SPSS® statistics for Windows version 25 (IBM, Armonk NY) and Stata© version 15 (Statacorp LP, College Station TX).

P-value of $< .05$ was considered statistically significant. When we tested the interactions in the mixed models, we used a significance level of $< .001$. This was due to the many tests, and using a significance level of 5% would have increased the risk of type I-error.

In both studies, the nine domains of the HLQ were used as dependent variables, and all domains were normally distributed. When testing our data, we compared the mean of continuous, normally distributed variables, using the Student's t-test. We used Pearson's correlation to test correlation between normally distributed continuous variables. A Mann-Whitney U test or Spearman's correlation were used in cases with skewed variables. To investigate categorical variables, we used Pearson's chi-squared test.

In paper I, we used linear multiple regression to find core variables associated with HL. The results were presented using the standardized beta coefficient (std.beta) that describes the relationship between the dependent and the independent variable using standard deviation. Using std.beta made it easier to compare the results across variables with different units, as the overall aim was to identify core variables associated with HL. The HLQ-scores were presented using the mean value of the HLQ-scores with 95% confidence interval (CI).

In paper II, we used linear mixed-effect models to identify changes in HL and describe the strengths of associations between the fixed factors and the change the HLQ-domains. Thus, unstandardized beta was presented. HLQ-scores were presented as margin values with 95% CI. The margin values are controlled for time and take into consideration that not all participants answered all the questionnaires. Conducting the linear mixed-effect models, time was used as a fixed, categorical variable. ID was included as a random effect, meaning that each participant had their own random intercept. Interaction effects between time and the fixed variables were tested one at a time.

In papers I and II, we chose to build the regression models using purposeful selection with backward elimination of variables. Purposeful selection is an explorative technique (141) involving statistical analysis to determine which variables to retain and which to exclude in the models. Since we knew little about the association between the different dimensions of HLQ and a variety of variables, purposeful selection made it possible to test a range of variables: sociodemographic variables (sex, age, civil status, and education), clinical variables (years of kidney disease, time in dialysis pre-transplantation, eGFR, rejections, comorbidity, and general health), transplant-specific knowledge and self-efficacy.

Purposeful selection with backward elimination is described in several publications, but we chose to use the method as described by Veierød et al. (142). The method starts by testing all independent variables in univariate linear regressions with the nine HLQ-domains as dependent variables. Variables with a significance level of < .20 were included in the multivariate model. After running the multivariate model, the variable with the highest p-value was excluded, and the model was run again. The procedure was repeated until all variables in the model had a p-value of < .05. Variables with a p-value of > .20 in the univariate analysis were then added one by one to identify variables that might become significant in the presence of other variables (143).

4.1.4.3 Assumptions of linear regressions and mixed models

When conducting linear regressions and mixed models, the methods make a number of assumptions about the data; to be able to interpret the results, we therefore needed to make sure that the data actually fulfilled these assumptions. In the analyzing procedures, we assessed the presence of any outliers, as this could interfere with the results. In the regression models, the residuals were normally distributed, and linearity was achieved (141). To test for multicollinearity, we tested the correlation of the variables that were first included in the regression models. None of the variables appearing together had a correlation above $r = .6$, which is acceptable (141). Another way of controlling for multicollinearity is to check for the variation inflation factor (VIF). According to Tabachnick and Fidell (141), the VIF should not exceed 3, which was not the case in any of the models.

4.1.4.4 Missing data

In the present study, we had missing data due to three different reasons. The first reason was that some participants never received the questionnaire at T1, T2, or T4; this was likely due to holidays, weekends, and busy periods in the clinic, and was therefore classified as missing totally at random, since that could have happened to anyone (144). At T3, everyone received the questionnaire by mail; here, missing data was due to responders not returning the questionnaire, and may be classified as missing at random. This involves that missingness is not due to the specific variable that is missing, but is related to another observed variable (144). We also had missingness due to the lack of permission to collect clinical information. Since data-collection was combined with another study, the informed consent for the present study did not include information about withdrawing clinical information, we therefore had to collect the proper consent by mail for the first 81 participants, whereas 52 participants returned the consent form. Missing of clinical data from 29 participants were also classified as missing at random. To identify any patterns in the missing data, we created an indicator variable (missing yes or no) and used it as an independent variable in a logistic regression analysis. Our analysis showed no systematic patterns of missing in our data. One of the strengths of using mixed models is that the method allows for inclusion of respondents that has missing units of the dependent variable.

In the table below, we have provided an overview of the response patterns for the questionnaires.

TABLE 5: Patterns of response on the questionnaires at all four time points

Frequency and percent	**Pattern**
102 (52.31)	Answered all questionnaires
20 (10.26)	Missing the first questionnaire
17 (8.72)	Missing the second questionnaire
15 (7.69)	Missing the fourth questionnaire
12 (6.15)	Missing the third questionnaire
8 (4.10)	Missing second and fourth questionnaire
7 (3.59)	Missing third and fourth questionnaire
6 (3.08)	Missing second and third questionnaire
3 (1.54)	Missing first, third and fourth questionnaire
5 (2.56)	Other pattern
195 (100)	

Missing variables in the HLQ were treated according to the authors manual, using the expectation maximization (EM) algorithm (145). Domains with four to five questions allowed for two missing values to be imputed. Domains with six questions allowed for three missing values to be imputed. In paper II, all missing data among the independent variables were treated with chained multiple imputation in StataMP15. This procedure involved imputing missing items 50 times, creating multiple “complete” datasets. The imputations are based on existing observations for each individual in addition to observed values for other responders. The procedure creates multiple predictions for each missing data and consider the uncertainty in the imputations (146). As such, including few variables in the imputation procedure will provide little information, and therefore produce more variability in the imputed values. If the imputation involve several observations that are predictive of the missing values, the imputations will be more consistent across the imputations (146). In the analysis, we included 14 variables for imputation. In addition, we included sex, age and the nine HLQ domains as basis information the for imputation. Multiple imputation operates under the assumption that the variables given in the procedure are missing at random, which was considered to be the case in the present study.

4.1.4.5 Effect size

With paper II, statistical significance would not necessarily give information about clinically significant changes in the HLQ domains. Although there are several ways to calculate clinical significance, Dodson et al. (145)$^{\text{Sheet 12}}$ recommend the use of effect size (ES).

ES was calculated by subtracting the margin values from each HLQ-domain at T2, T3, and T4 from the margins value from T1. The sum was then divided by the standard deviation of the specific HLQ domain from T1:

$$\frac{\text{margins value from each HLQ domain at T2, T3, T4} - \text{margin value at T1}}{\text{standard deviation for each domain from T1}} = \text{effect size}$$

A positive ES indicated improvement in HLQ scores and a negative ES indicated a decline. An ES of 0.20–0.50 was interpreted as small clinical significance. An ES of 0.50-0.80 was interpreted as moderate, and an ES of >0.80 was interpreted as large clinical significance (147).

4.2 Sub-study two: Exploring health literacy in kidney transplant recipients (paper III)

4.2.1 Designing the qualitative study

The objective of sub-study two was to explore HL in patients' experiences. To answer our research question, we used an explorative qualitative method involving observations and interviews. In our data gathering and analysis we were inspired by constructivist grounded theory (CGT) (148). During the first three weeks following a transplantation, the kidney transplant recipients has a close cooperation with health care providers, and several of the skills and competences related to HL are challenged in these interactions: e.g. finding, understanding, and using health information, critically discussing health issues, and engaging in consultations with health care providers. Therefore, we chose to observe two different types of consultations as a foundation for the first interview at three weeks post-transplantation.

To plan the qualitative study, we conducted a pilot study, in which I observed a patient education setting and conducted an interview at the surgical transplant ward. Furthermore, we had close cooperation with health care personnel at the outpatient ward, since this was the location for the observations and the first round of interviews. We had several meetings with the staff and arranged days when I could shadow the nurses and doctors in their daily routines at the ward. This provided input about relevant situations for later observations and contributions to the interview guide.

A user representative from the National Association for Kidney Patients and Transplant Recipients was involved in the planning and completion of the qualitative study. This was especially helpful when preparing for the observations and interviews. The user representative was also helpful in discussing the results of the interviews, as he could comment on whether the results were recognizable to him as a transplant recipient.

The observations and interviews were organized as follows:

- The first observation was conducted during a consultation with the nephrologist at the outpatient ward, 8-14 days following the transplantation.
- The second observation was conducted during a patient-education session at the outpatient ward, three weeks after the transplantation.
- The first interview was conducted a few hours after the last observation.
- The second interview was conducted about six months after the transplantation.

4.2.1.1 The interview guides

The WHO's definition of HL and the HLQ formed the basis of our multidimensional understanding of HL, and was an important starting point in our development of the first interview guide. However, we were open to exploring participants' experiences moving beyond existing definitions of HL. The interview guide contained several questions that had been prepared before the observations. To explore the specific experiences of each participant, questions generated from the observations were also included, for example concerning stories the participants had told and questions they had (or had not) asked.

In the second round of interviews, the interview guide focused on pursuing the codes and emerging categories from the first round of interviews. As with the first round of interviews, it was crucial to stay close to patient experiences, we were therefore inspired by the life-form interview, as described by Haavind (149). This approach is rooted in the participant's everyday life and concrete experiences (149, 150), and we were able to explore HL and emerging concepts through daily activities and any critical events that had happened since the previous interview.

None of the interview guides were strictly followed but instead I used them as a helpful tool for maintaining focus during the interviews. The interview guides are provided in the appendix (table S1).

4.2.1.2 Recruitment and sampling strategy

Recruitment for the study was undertaken at both the surgical ward and the outpatient ward 5 to 10 days after the transplantation. To be able to gather rich descriptions of what HL involved, we used purposeful sampling. In the present study, this involved recruiting participants with different socioeconomic and medical backgrounds to achieve maximum variation. We also used the HLQ to recruit participants with different HL strengths and limitations. Since we were to gather a rich amount of data from each participant, we planned to recruit a total of 10 participants.

The recruitment of health care personnel for the observational study was undertaken during the morning meetings at the outpatient ward. We also aimed to include different health care providers for the observations.

4.2.2 Data collection

4.2.2.1 Participant observations

Participant observation is located on a continuum, with only observing on one end (i.e. standing on the sidelines), and full participation on the other (i.e. being part of the context that is being observed) (151). When I began conducting the observations, I chose to take the observer role. This, however, proved more challenging than expected, since I became something of an alien in the room and it was clear that the participants were struggling to pretend like I was not there. As such, I decided to take a more active role as a participant, and emphasized in my introduction that the participants were free to speak to me during the consultations.

On the morning of the first observation, I had my first meeting with the participants. I met them wearing a white uniform to appear as a natural part of the environment. I introduced myself as a researcher and a nurse at the transplantation ward; however, I emphasized my role as a researcher in the present situation. In my introduction, I repeated the aim of the study and explained the construct of HL, using the Norwegian word "*helseforståelse*." I felt it was important to underline that I was only there to observe and learn from a normal consultation, and not to judge what took place during the consultation.

The observations were recorded to help me prepare for the interviews. In addition, I took notes about the interactions between the participants, and wrote down questions that might be relevant to ask during the interviews.

4.2.2.2 The interviews

The first interview took place a few hours following the final observation, three weeks post-transplantation. Most interviews took place in an office close to the outpatient ward, but in two cases, the participants asked if the interview could be conducted in their room at the patient hotel.

Before the interview, the participants were once again introduced to the aim of the study. HL was explained as follows: "HL involves how you seek, understand and use information relevant to your health. HL involves your experiences of social support, and interaction with health care personnel, and your experiences of navigating the health care system. Finally, HL involves the different decisions you make that might influence your health."

To schedule the second interview, I called the participants approximately two to four weeks in advance. I always began by asking the participants if they still wanted to participate in a second interview and the participant would choose where they wanted to meet. Eight of the participants invited me to their homes, one participant wanted to meet me in a café, and one wished to meet me at the hospital, where I had reserved an office. All the interviews were recorded.

TABLE 6: Overview of data collection in sub-study two

	Duration	**Recordings and notes**	**Location/ context**	**Time**	**Focus**
First observation:	13–35 min	Audio recording Field notes and questions for the first interview	Consultations with a nephrologist on the outpatient ward	8–14 days post-transplantation	Observation guide: non-verbal communication, atmosphere and potential questions for interview
Second observation:	25–45 min	Audio recording Field notes and questions for the first interview	The second patient education session on the outpatient ward with a nurse	3 weeks post-transplantation	Observation guide: non-verbal communication, atmosphere and potential questions for interview
First interview	40–110 min	Audio recording Field notes following the interview	1–3 hours after the second observation. In nearby office or in the participant's hotel room	3weeks post-transplantation	Interview guide and questions generated in the first and second observations
Second interview	75–150 min	Audio recording. Field notes following the interview	In the participant's home or at a place of their choice	6 months post-transplantation	Life-form interview with focus on everyday experiences. Interview guide generated by concepts emerging from the first interview

4.2.3 Analyzing the data

When we began collecting data for the qualitative study, I had not yet chosen the strategy for analysis. During data collection, I considered several analytical approaches; content analysis, narrative analysis, and hermeneutic or phenomenological analysis. Half-way through the first round of interviews, I decided to use constructivist grounded theory (CGT). The methodology seemed well-suited to our research question, as the aim of CGT is to generate theories regarding social phenomena and to explore processes in humans and in human actions. CGT presented a strong methodological frame that could guide both data collection and the analysis. At the same time, Kathy Charmaz, who developed CGT, emphasizes that CGT provides flexible and pragmatic guidelines rather than fixed methodological rules (148). CGT was therefore chosen as a methodological guide for further data collection and analysis.

CGT has its origin in grounded theory, which was developed by Glaser and Strauss in the 1960s (148), and it follows the inductive, emergent, open-ended, and iterative approach of grounded theory. An inductive method involves having a bottom-up approach, in which the analysis and results are based on empirical data, and not on existing theory. CGT is an emergent method, which enables the researcher to pursue research questions as they arise in the empirical material (152); data collection and analysis are thus performed with an open-ended approach, with no pre-defined expectations regarding findings. The iterative approach requires the researcher to move back and forth between collecting and analyzing data: data collection stimulates data analysis, analysis leads to the collection of additional data, which in turn leads to further refinement of the developing data analysis (148). CGT is a constant comparative method, involving the comparison within and across data, codes and emerging categories; by employing this method, CGT aims to illuminate both visible and hidden processes.

An important distinction between grounded theory and CGT is that CGT does not follow the positivist epistemology of Glaser and Strauss' earlier version of grounded theory, which treats data as an objective truth discovered by the researcher. CGT is built on the pragmatic heritage of Strauss, placing the method within the social constructivist tradition, in which data is understood as a co-construct between the researcher and the research participant (153). With his positivistic view of the world, Glaser believed that one should enter the field of research with no preconceptions and a blank mind. As such, he meant that reading about the field of research before entering it could bias the analysis. CGT has a different approach, which Charmaz has labeled "theoretical agnosticism" (153)[page 5]. With this approach, the researcher may read existing research and theory but should assess it with critical skepticism. Charmaz emphasizes the strength of doubting, which involves exploring what we take for granted, and dissecting our data, methods, and analysis (153). This doubting is part of the reflexivity encouraged by CGT. Reflexivity involves acknowledging and examining one's own assumptions about the world and how these might influence the research process (153).

In the research process, the coding and the data collection were performed simultaneously. The first phase of the coding began with a close, line-by-line reading of the transcribed interviews to generate codes that stayed close to the text. This initial coding phase (148) was followed by a more selective phase, in which the most significant or frequently occurring codes became focused codes. A code could be considered significant if it held importance for understanding the process of HL. The following quote (which is also used in paper III), illustrates this: *"I think I feel like I don't want to bother anyone. There are many things I have never asked about. But I know I have poor self-esteem and that it affects me in many areas"* (8-2). The focused code from this quote was low self-confidence, and was combined with other focused codes that concerned personal factors that could limit or facilitate HL. The focused codes were "tested" through constant comparison with the initial codes and other focused codes. In this process, memo-writing proved important in conceptualizing the emerging categories that became part of the model; this involved writing down the process of coding, comparing, recoding, and continuously questioning, commenting, and critically analyzing the process (148).

The focused codes and emerging categories from the first interview, such as triggers and the hierarchy of resources, were pursued in the second interview through theoretical sampling

(148). Theoretical sampling (as opposed to sampling to reflect population distribution, or sampling until no new data are generated (148)) was used to elaborate and refine focused codes and emerging categories; here, the goal was to reach saturation of the theoretical categories that appeared in the trigger-information-response model. The theoretical categories and the model were developed through constant comparison within and between codes, categories, memos, and the model.

The coding process was conducted in close cooperation and continuous discussions with Professor Eivind Engebretsen, one of my four supervisors, who has extensive experience with qualitative research. As the focused codes emerged, these were discussed further (and often) with all four supervisors. These continuous discussions were central in the process of analyzing and forced me to go back to the initial codes and focused codes to recode, redefine, and verify the theoretical categories and the final trigger-information-response model.

5.0 Data management and approvals

The research project was approved by the Norwegian Regional Ethics Committee (REK) (2016/1485/REK Sør-Øst C), by the data protection officer at Oslo University Hospital (Reference: 2016/14592), and by the head of the Department of Transplantation Medicine. Amendments for REK were filed twice during the process. The first of these was to obtain approval to conduct observations and interviews with the same participants, and to use a recorder during the observations (the original approval involved observing one group of participants and then interviewing another group). In the second amendment, we applied for approval to hand out the fourth and final questionnaire at the outpatient ward when the patients returned for their one-year follow-up, instead of mailing them.

The storage of all data, including audio recordings and transcribed material, was done through Services for Sensitive Data (TSD), which cooperates with OUS and the University of Oslo (UiO). OUS is responsible for the data in the study; as such, a cooperation agreement between UiO and OUS was signed to allow for the transfer of data from OUS to TSD. Data were stored in accordance with OUS' standards for storing research data. REK has granted permission to keep the data until 2027. After this, the data must be erased or anonymized.

5.1 Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki (154), the Norwegian laws on health research (155), and the Privacy Regulation and Personal Data Act (156). These ethical guidelines state that all medical research must ensure respect for the human subject and protect their health and rights, involving the researcher's duties to protect the dignity, integrity, right to self-determination, privacy, and confidentiality of the research subjects.

Potential participants for both of the sub-studies were provided with information, both orally and in writing. To minimize the potential influence of the researchers' interests, a nurse who was trained to obtain the informed consent conducted the recruitment. The informed consent process included the provision of information about the background and purpose of the study, and the right to refuse to participate or to withdraw consent at any time without reprisal. The source of funding was also disclosed in the written information. The potential risk associated with the study was considered to be minimal, however, the participants were informed that the study could be time consuming. All potential participants were informed that the data would be safely stored, and that only authorized personnel in the project would have access to the list of names associated with the data set. Further, all potential participants were informed that all published data would be anonymized, so that the identity of the participants would never be revealed. The written information also included contact information if participants had any questions about the study or if they wished to withdraw from the study.

In the qualitative study, the participants were invited to participate at either the surgical ward or the outpatient ward before they signed a written consent. Here, we considered it particularly important to inform the participants about the time expenditure associated with the interviews. In addition, as observing consultations with health personnel could involve examinations and the sharing of sensitive information, the participants' confidentiality was highlighted before the observations took place. The observations and interviews always began with the researcher asking openly whether the participants still wanted to participate in the study.

Any health personnel who were potential participants in the observations were informed about the study in two separate informational meetings – one for the doctors working at the outpatient and medical wards, and one for the nurses at the outpatient ward. On the morning before each observation, the information was repeated and potential participants were asked for their written consent. I attended the morning meetings in the outpatient ward on the day of the observation; this way it was possible to plan that the doctor or the nurse attending the observation had given informed consent.

During the data collection period for the present study, recruitment was taking place for another study also involving interviewing kidney transplant recipients above 65 years of age (157). To minimize the burden of several invitations to participate in various studies, the participants involved in the parallel study were not asked to participate in our qualitative sub-study.

During the second round of interviews, family members were present in three of the interviews. As both a researcher and guest in the participants' homes, it was more natural to include the family members than to exclude them. In two of the interview settings, the spouse of the participant was present during part of the interview. In the third interview setting, the participant was on paternity leave, and his one-year-old child was present during the interview. The possible influence of the family members was thoroughly discussed by the research group, which concluded that, in all three cases, the presence of these family members was part of the participants' normal everyday life and thus did not bias the results. As we had not been granted ethical approval for interviewing family members, any comments from family members were neither transcribed nor analyzed.

When submitting our paper to *PLoS One*, we were asked to share our data. This was problematic since sharing interview data would compromise the confidentiality of the participants. To be able to meet the journal's requirements, we consulted the data protection officer at OUS. The solution was to provide four interviews with key participants that were de-identified and processed such that any information that could reveal any identifiable information was removed. This included the location and names of local hospitals and health care providers, family members, ages, and diagnoses. Sections of personal stories were also removed to protect the participants from being recognized by former health care providers. In this way, we were able to protect the confidentiality and privacy of the participants.

To minimize the burden of participating in several studies, the questionnaires for the present study were combined with data gathering for another study ("Evaluating and Monitoring Evidence-Based Implementation of a Structured, Tailored Education Program for Renal Transplant Recipients"). The informed consent process of the other study did not include information about withdrawing clinical information from the electronic patient journal. We therefore had to send a revised informed consent form by mail to the first 81 participants.

6.0 Results

The next section provides the results of the three articles, starting by presenting the participants in the two sub-studies, then presenting each paper subsequently.

6.1 Participants and characteristics

In sub-study one, 199 kidney transplant recipients were included five days post-transplantation. Three participants were excluded, resulting in 196 participants (Table 7). The mean age was 56 years, and the median age was 58 years, with a 25th percentile of 47 years and 75th percentile of 66 years. The range was from 20 to 81 years, and 33 % of the sample were women. Using the Charlson comorbidity index, the participants had from 0 to 6 comorbidities, with a mean of 1.25. Of the 196 participants, 27% were transplanted with a kidney from a living donor, and 18 % had a history of earlier transplantations. Dialysis history showed that 39% were transplanted pre-emptively (before starting in dialysis), 18% had peritoneal dialysis, and 43% had hemodialysis before the transplantation. At 12 months, 2 participants reported that they needed dialysis, and 5 participants reported that their kidney function was not optimal. In our sample, 24% had experienced a rejection at some point during the first year following the kidney transplantation.

In the cross-sectional study, 159 kidney transplant recipients answered the HLQ at eight weeks post-transplantation. The sample age was the same as in the total sample of sub-study one (56 years) and 31% were women.

In sub-study two, 5 women and 5 men were invited to participate 5 to 10 days following the transplantation. Participants were between 28 and 78 years of age, with individuals in their 20s, 30s, 40s, 50s, and 70s. The participants came from different parts of Norway – some from cities, where future follow-ups would be at larger university hospitals, and some from rural areas, where follow-ups would take place in smaller local hospitals. The participants had different histories of kidney disease and different backgrounds regarding dialysis and donor status. The HLQ was also used to include kidney transplant recipients with different scores in the nine HLQ domains.

TABLE 7: An overview of the total sample of sub-study one and sub-study two. We provide mean and median even though the variables were normally distributed. The mean and median from paper I (eight weeks) deviate from paper II, due the different samples in the two papers. Tx is short for transplantation.

	Paper I				**Paper II**				**Paper III**	
Variables	**N**	**n (%)**	**Mean (SD)**	**Median (min-max)**	**N**	**n (%)**	**Mean (SD)**	**Median (min-max)**	**N**	**Range**
Age at time of TX (years)	159		56.1 (13.7)	58 (20-81)	196		56.0 (13.9)	58 (20-81)	10	28-78
Sex	159				196					
Women		50 (31.4)				64 (32.7)			5	
Men		109 (68.6)				132 (67.3)			5	
Ethnicity	159				196					
Norwegian		147 (92.5)				179 (91.2)			9	
Non-Norwegian		12 (7.5)				17 (8.7)			1	
Civil status	153				189					
Living with a partner		111 (72.5)				139 (73.5)			7	
Living alone		42 (27.5)				50 (26.5)			3	
Education	143				178					
Lower education		78 (54.5)				102 (57.3)			5	
Higher education		65 (45.5)				76 (42.7)			5	
Duration of CKD (months)	136		16.7 (14)	11 (1-55)	166		16.4 (13.6)	11 (1-55)		
History of TX	155				191					
First time		130 (83.9)				156 (81.7)			9	
Re-transplant		25 (16.1)				35 (18.3)			1	
Donor status	156				191					
Deceased donor		41 (26.3)				52 (27.2)			7	
Living donor		115 (73.7)				139 (72.8)			3	
Number of comorbidities	143		1.2 (1.3)	1 (0-6)	174		1.25 (1.4)	1 (0-6)		
Dialysis status pre-TX	143				174					
Pre-emptive dialysis		59 (41.3)				68 (39.1)			4	
Peritoneal dialysis		26 (18.1)				32 (18.4)			2	
Haemodialysis		58 (40.6)				74 (42.5)			4	
Months in dialysis	85		18.5 (13.3)	17 (0-74)	103		19.13 (13.0)	18 (0.25-74)		
Kidney function										
eGFR (mL/min/1.73m^2)	142		52.8 (15.5)	50 (14-106)	166		56.7 (19.2)	55.5 (11-112)		
Rejections										
8 weeks	141	19 (13.5)			188	25 (13.3)				
6 months					181	31 (17.1)				
12 months					161	38 (23.6)				
General health score [Scale range 1-5]										
At 5 days					170		3.1 (0.9)	3 (1-5)		
At 8 weeks	157		3.4 (0.9)	3 (1-5)	157		3.4 (0.9)	3 (1-5)		
At 6 months					160		3.2 (0.9)	3 (1-5)		
At 12 months					158		3.3 (0.9)	3 (1-5)		
Knowledge score [Scale range 0-14]										
At 5 days					172		10.0 (2.6)	10 (1-14)		
At 8 weeks	158		10.3 (2.6)	11 (0-14)	158		10.3 (2.6)	11 (0-14)		
At 6 months					163		9.9 (2.8)	10 (0-14)		
At 12 months					160		9.9 (2.7)	10 (1-14)		
Self-efficacy score [Scale range 10-40]										
At 5 days					166		32.2 (5.0)	32 (13-40)		
At 8 weeks	155		32.5 (4.6)	33 (22-40)	155		32.5 (4.6)	33 (22-40)		
At 6 months					161		32.0 (5.3)	32 (13-40)		
At 12 months					160		31.8 (4.9)	30.5 (18-40)		

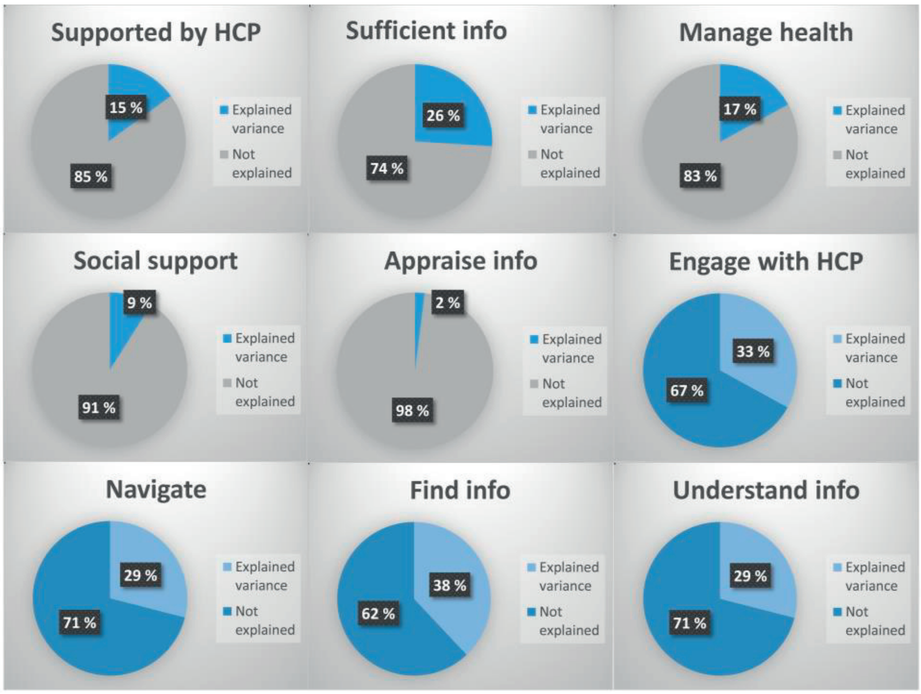
6.2 Sub-study one:

6.2.1 Identifying core variables associated with health literacy in kidney transplant recipients (paper I)

In the first paper, we aimed to investigate variables that could explain variations in HLQ scores at eight weeks following the kidney transplantation. Ten selected sociodemographic and clinical variables, self-reported health, transplant-related knowledge, and self-efficacy were fitted in one or several of the nine regression models. In domains 1–5, the regression models explained from 2% of the variability in "appraisal of health information" to 26% of the variability in "having sufficient information." In domains 6–9, the regression models explained from 29% of the variability in "navigating," and "understanding health information," to 38% of the variability in "finding good health information" (figure 4).

Three variables stand out as core variables that influenced variation in the HLQ domains: *self-efficacy* had the highest association with "having sufficient information" (std.β: .34, P=<.001), in domains 1–5, and "engaging with HCP" (std.β: .38, P=<.001) in domains 6–9. *Transplant-related knowledge* had the highest association with "feeling supported by HCP" (std.β: .28, P=<.001) in domains 1–5, and "understanding health information" (std.β: .29, P=<.001), in domains 6–9. *General health* had the strongest association with "social support" (std.β: .26, P=.001) in domains 1–5, and with "finding good health information" (std.β: .31, P=<.001) in domains 6–9. Sociodemographic and clinical variables were less associated with the HLQ domains.

FIGURE 4: show how much of the variability each of the regression models explained



In the first five domains, using a scale from 1–4, the participants had the highest scores in "feeling supported by HCP," while the lowest scores were found in "appraisal of health information." In the last four domains, using a scale from 1–5, the highest scores were found in "ability to actively engage with HCP," and the lowest scores were found in "navigating."

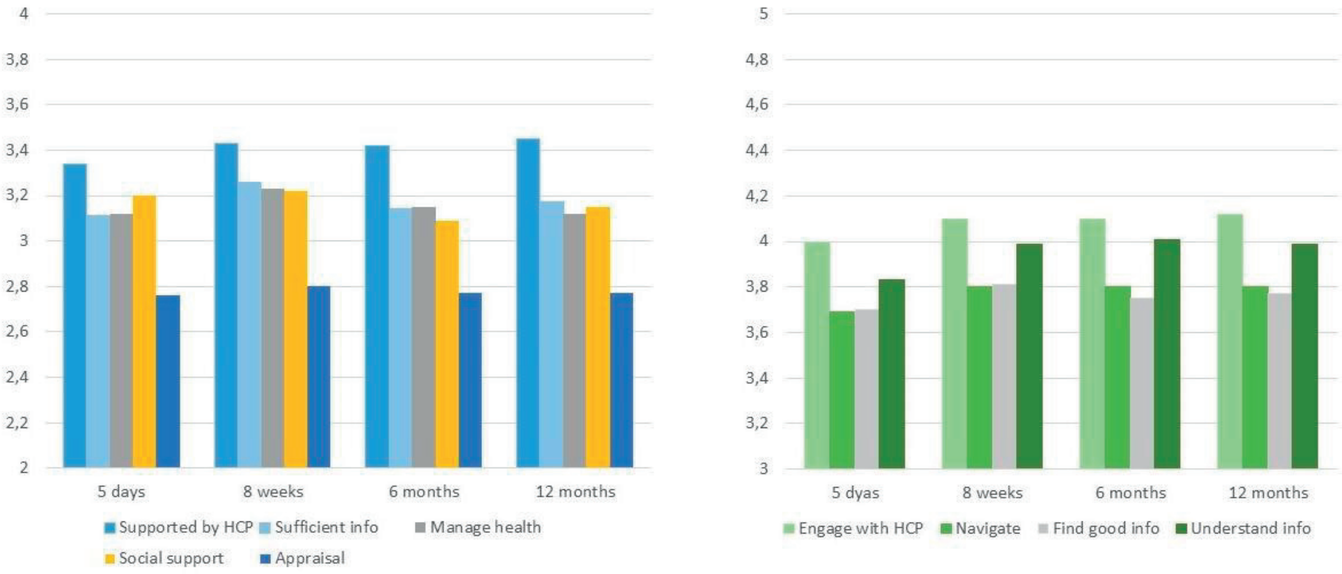
6.2.2 Changes in health literacy the first year following a kidney transplantation: using the Health Literacy Questionnaire (paper II)

In paper II, we aimed to identify patterns of change in HL during the first year post-transplantation, and to investigate the extent to which selected sociodemographic and clinical variables, general health, self-efficacy, and transplant-related knowledge were associated with HL during the first year post-transplantation.

We found statistically significant changes in eight out of the nine domains of the HLQ. The domain "appraisal of health information" was the only domain without any change. In "engaging with HCP," the scores had a steady increase with the highest score at 12 months. In "navigating" and "understanding health information," there was a significant increase from 5 days to 8 weeks, and the increase stabilized at 6 and 12 months. "Feeling supported by HCP" had a significant increase from 5 days to 8 weeks that disappeared at 6 months. However, a significant increase reappeared from 5 days to 12 months. In "having sufficient information," "managing health," and "finding good health information" there was a significant increase from 5 days to 8 weeks; however, there was no significant change from 5 days to 6 or 12 months. In "social support," we found a significant decrease from 5 days to 6 months. From 5 days to 12 months there was no significant change.

Using ES, we found *small* clinically significant changes in five domains: in "having sufficient information" and "managing health," there was a clinically significant increase from 5 days to 8 weeks. In "social support," we found a clinically significant decrease from 5 days to 6 months. In "engaging with HCP," there was a small clinically significant increase from 5 days to 12 months and in "understanding health information" all changes reflected a small clinically significant increase from baseline.

FIGURE 5: The bar chart presents the HLQ margin values throughout the first year post-transplantation. In domains 1–5, scores ≤ 2 involve "strongly disagree" or "disagree." Above 2 points, involve "agree" or "strongly agree." In domains 6–9, scores ≤ 3 involve "cannot do or always difficult," "usually difficult," or "sometimes difficult." More than three points involve "usually easy," or "always easy." We found the margin values to be above the critical low scores in all HLQ domains.



Self-efficacy and transplant-related knowledge were significantly associated with all HLQ domains, and general health were positively association with all HLQ domains except “appraisal of health information” and “understanding health information.” Clinical and sociodemographic variables showed less association with the nine HLQ domains (table 8).

TABLE 8: Markers (X) in black show associations with a significance level of < 1%, while markers (X) in grey show associations with a significance level of < 5%.

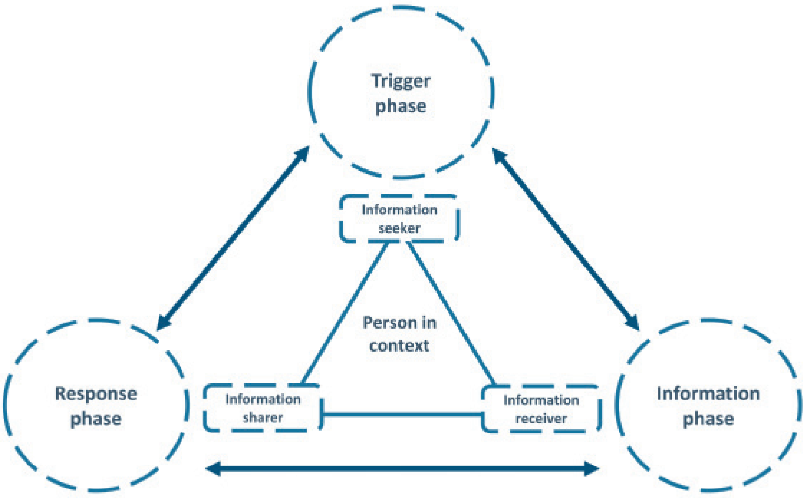
Independent variable	**Domain 1 Feeling supported by HCP**	**Domain 2 Having sufficient information**	**Domain 3 Managing health**	**Domain 4 Social support**	**Domain 5 Appraisal of health information**	**Domain 6 Engaging with HCP**	**Domain 7 Navigating**	**Domain 8 Finding good health information**	**Domain 9 Understanding health information**
Female		**X**	X						
Lower age					**X**				
Higher education								X	**X**
Living with a partner				X					
Less comorbidity		**X**							
More years of kidney disease	X						**X**	**X**	
Better general health	X	**X**	**X**	**X**		**X**	**X**	X	
More knowledge	**X**	**X**	X	**X**	**X**	**X**	**X**	**X**	**X**
Higher self-efficacy	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Number of groups (N)	**194**	**194**	**194**	**194**	**194**	**193**	**193**	**194**	**193**

6.3 Sub-study two:

6.3.1 The trigger-information-response model: Exploring health literacy during the first six months following a kidney transplantation (paper III)

In the third paper, our aim was to explore kidney transplant recipients experiences related to HL during the first six months post-transplantation. The main findings were presented as an empirical model consisting of a *trigger phase*, an *information phase*, and a *response phase*. The model illustrates HL as an active process that has no linear relationship between the three phases but instead moves within and between all three phases.

FIGURE 6: The trigger-information-response model



The participant was influenced by context and personal factors, and is visualized in the middle of this model as a receiver, seeker, and sharer of information. The *trigger phase* involved an experience that triggered the need for information or help, and could be caused by different kinds of information or bodily symptoms. The *information phase* concerned the handling and processing of information by using an individual hierarchy of information resources. In cases where the participants felt the need to seek information, they described how they worked with a hierarchy of resources based on contact, trust, and continuity. During the first interview at three weeks post-transplantation, the participants were living close to Rikshospitalet. The close relationship and access to expert knowledge resulted in health care providers being the primary source of information, while other information sources were considered less necessary. At six months, the context was very different, and increased distance from health care professionals allowed for other resources (e.g. the internet) to enter the hierarchy. Family members also became more important, especially in the process of discussing triggering episodes and in choosing an information resource. Most of the participants had placed specialist health care providers at the top of their trustworthiness list; however, there were several factors that could place other resources of information higher in the hierarchy. Personal factors like low self-esteem, not understanding the language of medical personnel, limited availability or lack of continuity of care could be factors that prevented participants from seeking information from health care professionals.

The *response phase* concerned the response to the trigger and/or the information that the participants had gained. It could involve health-related decisions, such as taking precautions to avoid infections or starting to exercise. During the second interview, the participants described how their responses had changed. Gaining more experience and increased knowledge about their own bodily reactions had adjusted their sensitivity towards certain triggers, and changed how participants assessed their need for information and what information resources they chose to use. Some triggers also remained the same, like fever, that would always make the participants call their local hospital. The participants were more aware of their changing sensitivity during the second interview (at six months following the transplantation), as they were unable to reflect on that development during the first interview (at three weeks post-transplantation). Both theoretical knowledge and bodily knowledge increased during the first six months following the transplantation. During the interview at three weeks, the participants focused on the more general knowledge that was associated with the patient education program. During the second interview, the participants reflected on knowledge that was more individual and related to their specific experiences.

7.0 Discussion

In the present study, the overall aim was to investigate multidimensional aspects of HL in the context of kidney transplant recipients. In the following section, I will discuss the main findings of the thesis, as well as the studies' contributions to the field of HL. Furthermore, I will continue to discuss the methodological considerations in my work and conclude the section with possible implications for clinical practice and future research.

7.1 Results

The integrated model of Sørensen et al. (14) focuses on the competencies needed in the process of *accessing*, *understanding*, *appraising*, and *applying* health-related information. The competences generate knowledge and skills that enable an individual to navigate the three domains of the health continuum: as a patient in the health care system, as a person at risk of disease, or as a healthy citizen promoting health. This thesis investigated the kidney transplant recipient as a patient in the health care system, but also as a person in the transition back home, where the transplant recipient must focus on disease prevention, side effects, and organ rejection (papers II and III). At the center of Sørensen et al.'s model, we find knowledge, competence, and motivation, which are personal attributes that are also found in the two sub-studies: in papers I and II, self-efficacy and knowledge, but also general health, were found to be associated with HL at eight weeks, *and* throughout the first year post-transplantation. In the qualitative paper (III), the trigger stands out as an important motivator, giving a more in-depth understanding of what encourages the process of accessing, understanding, appraising, and applying health-related information. Papers II and III show how different HL skills changed with time. Paper II showed small fluctuations in the nine HLQ domains consistent with a small effect sizes in five of the nine HL domains. Eight weeks seemed to be the time point with the highest scores, while six months seem to be a more challenging phase, where scores related to finding and having sufficient information and managing own health were no longer significantly higher than they were at baseline. Furthermore, the experience of social support had a negative development from baseline. It is possible that the levels of scores found at eight weeks were unrealistically high due to close follow-up during the first eight weeks. However, these findings may indicate that kidney transplant recipients need closer follow-up in the transition back home. Paper III revealed the development of other abilities related to HL, such as increased knowledge about how the body reacted to the new transplant and new medications. This tacit and intuitive knowledge was important to be able to know what to do and where to find help or information and reflect a different type of knowledge that was not captured by the HLQ.

Throughout the first year following the transplantation, the levels of HLQ-scores were over the critical low scores of 2 in domains 1–5 and above 3 in domains 6–9. In a recent Norwegian study of patients with CKD, stage 3–5, all HLQ-scores were lower compared to the present study sample (158). The results were from a single center study, and we are not able to generalize these results to the Norwegian population of patients with CKD. However, the comparison does support other findings that patients with pre-transplant CKD may have lower HL than patients receiving a transplant (113, 115). In a Canadian study, also using the HLQ in transplant recipients, the scores seem to be a little lower in domains 1–4, and slightly higher in domains 6–9 (22). However, Demian et al. does not provide the exact HLQ-scores or confidence interval and therefore does not allow for an exact comparison. Both Stømer et al. (158) and Demian et al. (22) found "appraisal of health information" to be the domain with the lowest scores, supporting our finding that this domain is more challenging.

The regression models in paper I explained at most 38% of the variability in "engaging with HCP", and only 2% of the variability in "appraisal of health information." As such, there are still many variables that need to be investigated in relation to HL in kidney transplant recipients. Nevertheless, kidney transplant recipients with low self-efficacy, less transplant-related knowledge, and lower self-perceived general health seem to be more vulnerable, with lower scores in several HLQ domains at eight weeks and throughout the first year post-transplantation. Even though self-efficacy is found in several theoretical models of HL (14, 159), research on the relation between self-efficacy and HL is rather scarce. Most of the studies we have found are in the field of diabetes care. Still, Caruso et al. (160) describe HL and self-efficacy as a knowledge gap in diabetes care, since the findings are inconsistent: some studies have found an association between self-efficacy and HL, and others have not. Xu et al. (161) also conducted a literature review on HL and self-efficacy in patients with diabetes, and found that 8 out of 11 studies identified a positive association between self-efficacy and all three of Nutbeam's three levels of HL (functional HL, interactive HL, and critical HL) (161). However, Xu et al. found that interactive and critical HL explained more variance in self-efficacy than functional HL. This could imply that individuals possessing interactive and critical HL in addition to functional literacy have higher levels of self-efficacy and more self-confidence in their self-care abilities (161). Different measurements of HL could also produce different results. When using subjective measures of HL, there is a possibility that the respondents with higher levels of self-efficacy overestimate their skills related to HL, and therefore rate their HL to be higher (161).

Transplant-specific knowledge were found to be associated with seven out of nine HLQ domains at eight weeks (paper I), and all domains during the first year post-transplantation (paper II). Other studies have also found disease-specific knowledge to be positively associated with HL (162-166). Undoubtedly, HL involves different kinds of knowledge. Definitions of HL often involve *skills*, *capacities*, or *resources*, which may be understood as certain types of knowledge. Other definitions involve more explicit inclusion of knowledge, like this definition by Plesant and Kuruvilla: *"Health literacy is thus a skill-based process individuals use to identify and transform information into knowledge. This communication process inherently involves decoding a symbol system such as printed words, spoken language or visual elements and placing that information into a useful context"* (93)$^{p.154}$.

Willis et al. (167) describes several types of knowledge required to be able to navigate the health care system. "Navigation" involves what Willis et al. would describe as "system knowledge," which is knowledge about how a specific system works, how to navigate the system, and when and how to apply the unspoken rules of the system (167). System knowledge was found in both of the sub-studies. In sub-study one (papers I and II), it was found in the domain "navigation," but it may also be reflected in lengths of kidney disease – a variable that was positively associated with several HLQ-domains. Furthermore, Willis et al. describe self-knowledge (167), which is the knowledge of the experienced chronic patient that involves knowing one's body and how it responds in different contexts. Self-knowledge became more evident in sub-study two (paper III) as the personal bodily intuition and tacit knowledge about what triggers to react to and which ones to ignore. This type of knowledge is not often explored with available HL tools. In a review study of qualitative studies, Jamieson et al. (65) also describes this intuitive knowledge in transplant recipients, and how it developed with time and experience (65), and thus it is not new knowledge. However, it is important to put this knowledge in the context of HL, as it advances our understanding of HL. In the context of kidney transplantation, different symptoms may be difficult to assess and place; hence, this bodily knowledge is a crucial HL skill.

In papers I and II, we found that participants with less transplant-specific knowledge had lower scores in domains related to interaction with health care providers. Several papers have found that health care providers overestimate their patients' level of HL (168, 169), and Easton et al. (110) found that patients were often able to conceal their low literacy by avoiding engagement with health care professionals. In paper III, we found that low self-esteem could limit contact with health care professionals, and keep participants from taking their time and utilizing the consultations. The same mechanisms may be present when assessing a patient's level of knowledge. If the participant is relatively passive and the teacher does not actively seek the patient's knowledge gaps and needs, patient education can become a monologue, where the patient is only a listener. Employing an approach like the teach-back method may offer a way to identify the level of knowledge in kidney transplant recipients. The teach-back method is an evidence-based method in which the health care provider asks the patient to repeat the information they have been given in their own words (170). This way, health care providers may identify any misunderstandings and be more confident that the information was tailored to the recipient's needs.

The association between poor health and low HL has been found in several studies (71, 72, 81, 171-173). In the context of kidney transplant recipients, studies have focused on objective measures of health and found lower HL-scores to be associated with higher blood pressure (122), higher creatinine (18, 22) and lower eGFR (22). In the present study, objective measures, such as eGFR, rejection episodes, and postoperative complications were less associated with HL while the subjective perception of health were found to be associated with several HLQ domains in sub-study one. These findings might have several explanations. First, we included few objective measures of health at six months, and we did not measure the experience of medication side effects at any time. The variable general health showed a significant increase from five days to eight week post-transplantation, but did not show any significant change from five days to six months. As such, it is natural that the experience of poor health will increase the need for information and challenge the ability to manage health, find information and navigate.

Secondly, self-perceived health might be associated to the transplant recipients' expectations of post-transplant health. Schulz et al. (174) found that kidney transplant recipients had higher expectations related to their quality of life before the transplantation, than what they reported after the transplantation, especially related to physical quality of life. Crawford et al. found that the transplant waiting list could be seen as a *"route to normality"* (175)$^{\text{page 1206}}$, and unrealistic expectations of life after the kidney transplantation did not prepare the transplant recipients for the challenges they could face in the first few months (175). These studies might indicate that health care providers should discuss expectations related to the transplantation, both before and after the transplantation. The association between social support and general health also reveal the need to include family members in pre and post-transplant follow-up.

"Appraisal of health information" stands out as the domain with the lowest scores and as the only domain with no changes during the first year following the transplantations. This finding may be interpreted in several ways. The patient education provided during the first eight weeks may have had little focus on critically assessing health information. In addition, some participants may have found it challenging to ask critical questions due to a health care system that remains characterized by hierarchical structures. Another explanation might be that many recipients may have obtained most of their information from their nephrologist. In the qualitative study, the participants described how they arranged their information resources in a hierarchy, in which the nephrologist was often positioned at the very top. If information comes from a specialist, it may be less relevant for the recipient to doubt or question the information. In the context of kidney transplant recipients, "appraisal of health information" may therefore not give us accurate knowledge about whether transplant recipients critically assess health information. As such, a relevant follow-up question would target how kidney transplant recipients assess *different* sources of information, as they may assess information from the nephrologist and information from other sources differently.

In paper III, the results were presented through a model describing three phases: the trigger phase, the information phase and the response phase. A model, though based on empirical data, will always reduce and simplify human nature and behavior. However, the model in paper III might have helped us identify some important aspects related to HL: the trigger as an important motivator for seeking, sharing, and receiving information; the hierarchy of information resources; and the development of theoretical and bodily knowledge that result from personal experiences and needs. During the first six months, contexts and personal experiences changed; as such, both the participants' experiences of triggers and their access to health information changed. These changes also influenced their decisions related to HL.

An important question is whether the trigger-information-response model provides new insight to existing models of HL (for example, those of Sørensen et al. and Chisholm-Burns et al.) Sørensen et al.'s integrated model of HL (14) is perhaps one of the most used models today, as it incorporates several other models, and involve dynamic and multidimensional aspects of HL. Chisholm-Burns et al. (176) conducted a review of the literature on HL in solid organ transplantation and adapted the model of Paasche-Orlow and Wolf (159); this model focuses on the causal pathway linking HL to health outcomes in transplant recipients. One limitation of these two models is that neither involve the experiences of the patient. Sørensen et al.'s critique of existing models is that very few have been validated empirically (14). The model presented in paper III is based on the patients' experiences, and provides novel insight into the mechanisms that influenced the 10 transplant recipients in their daily health-related decisions. The results are clinically relevant, as the trigger may be used as a tool in patient education and in understanding what motivates (or does not motivate) the patient to seek, receive, or share information. Furthermore, exploring the hierarchy of information resources generated important insight into how the participants chose one source of information above another. We found that low levels of trust reduced the chance of using a particular source of information. Not understanding the health care provider, poor availability, and lack of continuity could constrain and reduce the chance of using health care providers to gain information. A Taiwanese study of the general population showed that higher levels of HL were associated with higher levels of trust in physicians and in the health care system (177). Chen et al. (178) also found, in an American population, that participants with lower levels of HL had less trust in specialist doctors and more trust in sources like television, social media, or information found online. These results may indicate that the most vulnerable patients may also be the hardest to reach, which again emphasizes the necessity of exploring the mechanisms behind HL and make health care accessible for everyone.

7.2 Methods

Validity concern whether we can trust the results of a study (179). As Polit and Beck state: *"Validity is always a matter of degree, not an absolute"* (179) $^{p.286}$. It is therefore important to reflect on possible biases that may have influenced or impaired the validity of our study.

7.2.1 Validity and reliability of outcome measures

Validating a questionnaire involve evaluating whether the measurement actually captures the targeted concept. The questionnaire should be able to reflect the definition of the concept and cover all relevant aspects (180). Jordan et al., (181) conducted a review of the development and content of existing measures of HL from 1990 to 2008, and concluded that most measurements did not consistently measure HL according to existing definitions. The HLQ was developed to capture the full breadth of multidimensional definitions and to meet the psychometric weaknesses found in existing measurements (100).

The HLQ has been validated through several studies and in several languages (182-184), and has been found to have strong psychometric properties and to be a good measure of HL (182, 185, 186). The Norwegian translation of the HLQ followed strict procedures to ensure a linguistically, culturally, and psychometrically robust translation (131). The questionnaire was recently validated in a Norwegian population of first-year nursing students. The results indicated the HLQ to be a robust measure of HL, but with some possible overlap between "navigating" and "finding good health information" (132). In the present study, we used Cronbach's alpha to assess the internal consistency and scale reliability at all time points. The alpha score was .76 at the lowest and .87 at the highest, indicating good internal reliability (180).

One of the most important strengths of the HLQ is that it covers nine independent domains of HL, giving one score for each domain. Most other measures of HL give one total score, and do not allow for the complexity of HL to appear in the same way. The HLQ gives information that reflect HL weaknesses and strengths both in the respondent, but also the health care system. As such, the HLQ constitutes a good foundation for planning future interventions that are meaningful in the context of kidney transplantation.

Kiechle et al. conducted a systematic review on studies using both performance-based and self-reported measures. They argue that there is an important difference between objective and subjective measures of HL, as they measure different constructs (187). The authors argue that self-reported measures of HL (such as the HLQ) assess participants' confidence in their

HL capacities more than they measure actual HL abilities. Another meta-analysis, investigating the association between HL and diabetes outcomes, found that knowledge about diabetes was best predicted by objective measures of HL, while self-care behavior was best predicted by subjective measures. Considering glycemic control, both objective and subjective measures gave the same results (166). Whether to choose a subjective or objective measure of HL depend on the research question. The purpose of the present study was to gain knowledge about patient experiences. Using the HLQ has therefore provided valuable information that may inform future interventions.

The GSE has been translated into several languages and applied in a variety of cultural settings (134, 137). In the present study, the alpha scores ranged between .90 to .93, indicating good internal reliability. The Knowledge Questionnaire for Renal Recipients was developed for the Norwegian context and was therefore a good measure of transplant-related knowledge in the present study. However, the questionnaire might have some weaknesses related to the design. The respondents were presented with fourteen statements and “totally disagree,” “disagree,” “neither disagree nor agree,” “agree,” or “totally agree” as possible responses. When calculating points, only respondents answering “totally disagree” or “totally agree” were given points. The alternatives “agree” or “disagree” were thought to reflect uncertainty. However, it may be problematic to make this definitive distinction between “totally disagree,” and “disagree,” and between “agree,” or “totally agree,” since both answering alternatives could reflect the right answer. It might also be possible that those who answered “totally disagree” or “totally agree” could have been participants with a higher degree of self-efficacy and belief in their own knowledge.

Regarding the single question about health, it has been found to be a useful indicator of patient wellbeing (140). Although it does not give us an objective or detailed understanding of the respondent’s health condition it has been found to predict health outcomes (188). However, the questionnaire does not provide information about whether the respondent base their answers on their illness, their physical or psychological function (189). Having a kidney transplant most likely comes with certain expectations regarding health, and these expectations may influence self-perceived health.

In the weighing of comorbidity, we considered several indexes: the Charlson comorbidity index, (190), the Davies comorbidity index (191) and the Liu comorbidity index (192). The latter two indexes were developed specifically for patients in dialysis. However, none of these indexes covered all diagnoses found in the study population, e.g. neurological diseases or mental disorders. Due to the complex work of weighing diagnoses without following an index and possible inconsistency in reporting all relevant diagnoses in the electronic patient journal, we chose to use the Charlson comorbidity index. This index is also found in several other studies of HL, and enables comparison across different studies. Due to the exclusion of some diagnoses found in the electronic patient journals, this might also have biased the results.

With regards to the variable organ rejections, we used information from the electronic patient journal at eight weeks. However, at 6 and 12 months we used self-reported data. This resulted in a rejection rate of 23.6%, which is above the rejection rate reported in the literature (39). We chose to use the self-reported data, since information about any rejections during the first year was not always available through the electronic patient journal at OUS. It is, however, plausible that some participants did not report, or reported a rejection that was not classified as a rejection according to diagnostic criteria.

During the selections of independent variables, we excluded some variables due to low quality. We planned to measure level of adherence by observing whether the participants had written down their weight, temperature, and fluid balance in their transplantation diary. However, the quality of these data was poor and the risk of bias was high, as some participants were told that they no longer needed to register fluid balance. Adherence was therefore not included as an outcome measure. Patients with new onset diabetes after transplantation (NODAT) was also excluded as a variable, since the diagnosis was not sufficiently described in the available patient journals at OUS.

7.2.2 Missing data

Missing data may cause selection bias in a quantitative study and it is therefore important to discuss the presence and possible influence of missing data (179). In sub-study one, 111 patients were not invited to participate in the study, comprising 31% of the patients receiving a kidney during the recruitment period. The reason for this was that during busy periods and holidays there was less focus on including patients. Due to ethical constraints, we were unable to gather information about patients who were not included in the sample. As such, we do not know if they deviate considerably from the sample. However, we do know that not receiving an invitation was random, since it relied on the capacity in the ward, and not on the patient.

As discussed earlier in the thesis, the participants who agreed to join the study had both missing units (questionnaires) and missing items (single questions). We know that several of the participants who were included never received the questionnaire at one or several time points, leading to missing units. Since this could happen to anybody, these missing units were considered to be missing totally at random. At 6 months, the questionnaires were sent by mail and the response rate was 84%, and higher than it was at 8 weeks (81.5%) and 12 months (82%). However, at six months (T3), missing units were due to the participants not returning the questionnaires. Comparing the responders with non-responders at 6 months revealed a significant deviation in age (responders: 57 years; non-responders: 49 years); this deviation was not found in responders versus non-responders at T1, T2, or T4. Since there were more missing units among younger participants, this would be categorized as missing at random, since missing is caused by the independent variable age (144).

In sub-study one, we had several missing items in the independent variables, which caused participants to fall out of the regression analysis in paper I. In domain 7, “navigating,” we see that there are only 114 participants included in the final analysis, even though 159 participants had answered the questionnaire. This exclusion might have caused selection bias that influenced our results, (if the missingness was not completely at random).

To avoid exclusion of participants with missing information in the independent variables, missing data was treated with multiple imputation in paper II. After conducting multiple imputations, the sample size was between 193 and 194 respondents, while it varied from 160 to 194 before imputation. The imputation did not influence changes in the HLQ-domains, since we only imputed the independent variables. However, results from the imputed data deviated slightly from the non-imputed data, in terms of variables associated with the HLQ-domains. In analysis with imputed data, less significant variables (from the analysis before imputing) fell out of the analysis, while general health became significantly associated with “supported by HCP,” with a significance-level of < 5%. General health became more significantly associated with “engaging with HCP,” and knowledge was more significantly associated with "finding good health information." Tables showing analysis before and after imputations are provided in the appendix (S2 and S3).

7.2.3 Statistical validity

In the first sub-study, we used the nine domains of the HLQ as dependent variables, which caused many analyses, and consequently many statistically significant results. In several fields of research, there is a common understanding that results with a P-value of < 5 % is considered statistically significant (193). The P-value indicate the probability of obtaining the observed results or more extreme observations, assuming that the 0-hypothesis is correct (142). However, 5% significance involve that one out of 20 result are false positive, resulting in rejecting the 0-hypothesis when we should have kept it. This type of error is known as type-I error. Since we did many analyses in our study, we chose to focus on results having a significance level of 1% to minimize type 1-errors (193).

To ensure a sufficient sample size that enabled us to perform the planned analysis, we conducted a power analysis. If the number of participants had been too few, we might have failed to achieve statistical significance and thus have decided to keep the null hypotheses (i.e. that none of the independent variables were able to explain any variance in the HLQ scores). This type of error – rejecting the alternative hypothesis when one should have retained it – is called a type II error (194). The power analysis showed that our sample size was adequate to conduct the planned analysis.

Effect size was calculated to be able to assess the clinical significance of the results in paper II. Clinical significance involves the minimal important difference or the smallest changes in the scores considered to be meaningful to the respondent (147). In paper II, this was an important assessment to evaluate the clinical impact of the results. The results only involved small effect sizes; however, by using ES we might assume that these differences involved a clinical significant change for the participants. Ferguson et al. (195) emphasize that effect size is just estimates and depend on several considerations, such as the quality of the measurement and the sampling strategies. The HLQ has been validated in several contexts' and found to be a robust measure of HL. Further, our sampling strategy aimed at inviting all patients receiving a kidney in the recruitment period, and patients not receiving an invitation was due to the capacity in the ward and therefore random. These considerations strengthens the results of the ES calculations. However, within four HLQ domains, we found changes with an ES between 0.16 and 0.19. Whether these results may comprise a clinically significant change for the participants, we are not able to say.

7.2.4 External validity

External validity concerns the degree to which the research results may be generalized to other relevant populations (179). In Norway, there is only one national transplant center, which enabled us to collect data from a sample representing all kidney transplant recipients in Norway. To evaluate the generalizability of the study, we compared our sample with transplant recipients receiving a kidney between 2016 and 2017, since the recruitment process took place between February 2016 and August 2017. In 2016, 222 patients received kidneys alone (16 were simultaneously transplanted with a kidney and a pancreas, while two received a kidney in combination with a liver) (196). In 2017, 261 patients received a single kidney (11 had a combined kidney and pancreas transplantation and two patients had a combined kidney and liver transplantation) (37), (table 9).

*TABLE 9: Distribution of kidney transplant recipients from 2016 and 2017, for comparison with the study sample. The numbers are based on the annual report from the NNR (37, 196). *We did not know the donor status in five participants.*

	2016		**2017**		**Present study (Feb 2016 – Aug 2017)**	
	N (%)	***Median age***	***N (%)***	***Median age***	***N (%)***	***Median age***
Deceased donor graft	175 (79%)	54	184 (70%)	57	139 (73%)	59
Living donor graft	47 (21%)	45	77 (30%)	50	52 (27%)	55
Regraft recipients	32 (14%)	52	45 (16%)	56	35 (18%)	55
Total number of kidney transplant recipients	222		261		191*	

Comparing the number of kidney transplant recipients in 2016 and 2017, and the distribution of patients that had a re-transplant or had received a kidney graft from a deceased or living donor, we see that the study samples are similar. Considering median age, the sample population with living and deceased donors were slightly higher. However, we do find it possible to generalize our findings to other Norwegian transplant recipients.

The number and distributions of deceased and living donors in Norway is similar to other Scandinavian countries, as are the number of patients on the waitlist (197). Furthermore, our health care systems are quite similar. As such, our results may also be generalized to kidney transplant recipients in other Scandinavian countries.

A substantial limitation in our study is our exclusion of 25 kidney transplant recipients who were not able to answer a Norwegian questionnaire. This limits our external validity, and we are unable to generalize our results to non-Norwegian speaking kidney recipients.

7.2.5 Trustworthiness in the qualitative study

There is an extensive body of literature on how to assess validity and reliability in qualitative inquiry, demonstrating a range of ways to ensure rigor during the research phase and when reporting the results (198-202). Lincoln and Guba have presented five strategies to ensure trustworthiness that I make use of in the methodological discussion: *credibility, dependability, confirmability, transferability* (203), and *authenticity* (204). *Transparency* and *reflexivity* (201) are also important concepts when evaluating the research quality and will be mentioned briefly in relation to our study.

Credibility refers to confidence in the truth of the data and whether the analysis and results actually reflect the participant's true story (203). CGT provides a methodology that ensure credibility in several ways. Line-by-line coding (148) ensured that all parts of the interview materials were investigated thoroughly and thereby prevented premature interpretations. Constant comparison (148) involved going back and forth, comparing codes with codes, and codes with theoretical categories to ensured depth in the understanding of the data. Using theoretical sampling (148) and having the opportunity to interview the participants a second time gave us the chance to "test" the analysis from the first round of interviews, and get richer descriptions of the codes. It also allowed for a trustful relationship between the participants and me as the researcher, since we met several times over the first six months. Both constant comparison and theoretical sampling are methods that increase credibility.

Dependability aims to ensure that the interpretations of the data were not based on my own preferences, but were grounded in the data (203, 205). Dependability may be ensured through transparency and descriptions of how the study was conducted. Wringing memos was helpful to achieve dependability as I could track the study process. Analyzing the data was conducted through continuous discussion with experienced researchers. This was important to achieve conformability (203), or congruence about the analysis and increased the dependability of the findings. The findings were also discussed with the user representative (from the National Association for Kidney Patients and Transplant Recipients), who recognized the theoretical codes as important and relevant to HL following a transplantation.

Authenticity refers to the extent to which the results fairly and faithfully show a range of different realities (204). The sample in the qualitative study had a large variation and we gathered rich data through two rounds of interview. This enabled us to cover several unique perspectives related to HL.

Transferability involves in what degree others may find the results to be transferable to other situations or other people (201, 205). This require sufficient and rich details about the specific phenomena and also rich descriptions of the participants (203, 206). Furthermore, transferability require transparency, so that other researchers may evaluate whether the methods, the participant's and the results may be transferable to their area of inquiry (205). To make it possible for other researchers to assess the transferability of the results, we described the study process, provided the interview guides, described the patients and their background and the context of the different interviews. However, the degree of transferability is not for the researcher to judge, but the reader (205).

In qualitative research, we know that the researcher will always influences the process in different ways. Malterud states that *"the question is neither whether the researcher affects the process nor whether such an effect can be prevented."* (201) $^{p.484}$. Furthermore, using CGT, findings are considered to be a co-construct between the researcher and the participant (148). When conducting qualitative research, the researchers must therefore evaluate their own effect on the process – also known as reflexivity. To achieve reflexivity, we provided information in the paper about my background, and how the study participants were introduced to me as both a nurse and a researcher. We emphasized that the researcher did not have contact with the participants while they were in the surgical ward, since this could lead to role confusion. As I conducted the interviews and the analysis, I had to be aware of my own assumptions and my own understanding of HL, since this would influence both the interviews and the analysis. I was rather new to HL during this phase; however, I was critical of the normative focus that HL can take, describing behavior as "good" or "bad." Hence, the interviews did not focus on evaluating or judging the decisions that the participants made following the transplantation, but openly asked about experiences related to HL, to understand the processes involved in HL.

8.0 Conclusion

In this thesis, our overall aim was to investigate HL in kidney transplant recipients through two sub-studies. In sub-study one, our objective was to identify whether selected variables were associated with different aspects of HL eight weeks after the kidney transplantation. Furthermore, we aimed to investigate possible patterns of change in HL during the first year following a kidney transplantation, and variables associated with HL throughout the year. In sub-study two, our aim was to explore kidney transplant recipients' experiences related to finding, understanding, and using health information, and making decisions about their health during the first six months post-transplantation.

Using multiple methods has given us the opportunity to capture a large amount of data and a complex and multifaceted understanding of HL in the context of kidney transplant recipients. Despite some weaknesses in our study, we find the results to be valid and trustworthy, and to provide novel insight into the HL of kidney recipients.

In paper I, we found the highest scores in domains related to interaction with health care providers, while the lowest scores were found in "appraisal of health information" and in "navigating." We identified participants with lower self-efficacy, lower levels of transplant-related knowledge, and lower levels of general health to be a more vulnerable group with regards to several HLQ domains at eight weeks post-transplantation.

In paper II, we identified two main patterns of changes in the nine HLQ domains: a) domains with a significant increase throughout the first year ("engaging with HCP," "navigating," and "understanding health information"), and b) domains with a significant increase from 5 days to 8 weeks that were no longer significantly different at 6 and 12 months ("having sufficient information," "managing health," and "finding good health information"). Three domains had patterns that deviated from the two main patterns: "feeling supported by HCP" also had a significant increase from baseline to eight weeks that disappeared at six months. However, a significant increase reappeared at 12 months. "Social support" had a significantly negative development from baseline to six months and "appraisal of health information" had no significant change. Furthermore, self-efficacy, transplant-related knowledge, and general health were found to be core variables associated with HL during the first year post-transplantation.

In paper III, the results were presented through the trigger-information-response model that consisted of the following phases: the trigger phase, the information phase, and the response phase. HL was presented as an active process that was continuously influenced by context and personal factors. The study provides insight into what motivated the participants to find, share, and receive information. Furthermore, the study illuminates how the transplant recipients made decisions about using different sources of information. For some participants, personal factors like low self-esteem, accessibility, and continuity of care could prevent them from seeking information from health care professionals.

8.1 Implication for practice

This thesis consists of several results that may inform future research and practice in kidney transplant care. The results from sub-study one (papers I and II) identified self-efficacy, transplant-related knowledge, and self-perceived health to be core variables associated with HL. These factors should be emphasized in future kidney transplant follow-up, as they may strengthen or limit aspects related to HL. Health care personnel might discuss expectations regarding self-efficacy, coping with problem-solving, and relevant challenges following the transplantation. Concerning the current patient education program, it may not be designed to identify patients with lower levels of knowledge or HL limitations. As such, the use of teach-back methods could provide nurses with a useful tool to identify knowledge needs or any misunderstandings of information. Furthermore, identifying the patients' own perception of their health might reveal unexpressed HL needs or unmet expectations. Additionally, these factors are not only important during the first eight weeks post-transplantation, but should gain continuous focus throughout the first year.

During the first year as transplant recipients, finding and having sufficient information and managing health had a negative trend from 8 weeks to 6 and 12 months. These results may indicate that transplant recipients need closer follow-up for a longer period than is currently the norm, as different health challenges may occur later in the post-transplant phase. For example, following lifestyle recommendations is known to be challenging, and transplant recipients may need closer follow-up to be able to adhere to these recommendations.

Critical appraisal of information had the lowest scores of the nine HLQ domains, and did not change during the first year post-transplantation. The current transplant follow-up has little focus on educating patients to be active and critical users of health information. However, this domain reflects important skills, since the amount of available information sources is increasing extensively. Health care providers should take the initiative in helping transplant recipients enhance these abilities, as they often have a close relationship with their kidney transplant patients. The qualitative study in this thesis showed how reduced availability and lack of continuity in care could prevent the participants from seeking information from health care professionals. Focus on continuity in follow-up may be key to developing trusting relationships between patients and their health care providers; this in turn may increase the likelihood that the patients will turn to health care professionals to discuss their challenges instead of using other information sources, like the internet. Transplant medicine is a complex field of medicine and a good relationship between health care providers and the transplant recipient is essential.

Social support had a significant decrease from baseline to six months. In the current practice, patient education and follow-up do not focus on including next of kin. Transplant recipients are often away from their home context for the transplantation and the eight weeks of transplant follow-up. Focus on including family members or other significant people may be important to strengthen patients' experience of social support in the months that follows. Including family members may also provide the opportunity to discuss and possibly adjust expectations related to the transplantation. This is essential because the patients' level of self-perceived health may be related to certain expectations following the transplantation. As such, having an open dialogue about expectations, involving both the transplant recipient and their families, may be an important part of pre -and post-transplant follow-up.

8.2 Implications for research

While the findings from this thesis answered our research questions, new questions and implications for future research also emerged.

The domain “appraisal of health information” may benefit from a deeper investigation in the future to explore how the respondents explain their answers. As this domain does not differentiate between different information sources, we do not know whether respondents had low scores because they did not *need* to critically assess the information provided, or because they found the appraisal of health information challenging.

In the present study, we did not include patients who were unable to answer the Norwegian questionnaire. As this might have excluded a vulnerable group with regards to HL, future Norwegian studies should focus on non-Norwegian-speaking kidney transplant recipients.

Furthermore, future research and interventions should focus on how to easily provide accessible information. Technological devices like online resource groups, led by health professionals, or apps may be a solution to facilitate easy access to information of good quality. There is also little knowledge about how the health care system can better facilitate HL in transplant recipients and other groups of patients. Future research should therefore investigate how health care organizations provide services to patients with different HL strengths and limitations. Initiatives to meet the patients’ needs should further be systematized as quality indicators in future health care.

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Appendix

TABLE S1: Interview guide 1 and 2: In interview 1, examples of possible questions from the observations are written in brackets [ ]. In interview 2, themes that we pursued from interview 1 are written in parenthesis.

Interview guide 1

The observations were used to tailor the questions and to generate additional questions relevant to the research question. The interview guide was used as a base to open up for other experiences related to health literacy. Examples of follow-up questions in parenthesis.

- **Can you describe how you have experienced the consultations and teaching situations with the health care providers so far?**
  [From the observation: How did the patient behave? Did he/she look strained/comfortable?] (Does the participant have any other experiences with receiving health information or patient education?).
- **Was it easy to understand what the nurse or doctor meant/ was there anything that was hard to understand?**
  [From the observation: Did the doctor/nurse use difficult words? Did the participants have any questions?] (Do the participant have relevant experiences from other situations?).
- **What did you get out of the consultations/ patient education?**
  [From the observation: did the participant seem interested during the consultation? What information was meaningful to the participant?]
- **Did you feel motivated for patient education?**
- **(What motivates you to receive information?).**
- **What is important to you when you receive information or patient education?**
- **Have you had any questions during any of your consultations that you did not ask?**
  [From the observation: did the participants have any questions?]
- **Are there any topics that are difficult to talk about or to ask about?**
- **Are there any thing in your daily life that make it difficult to concentrate on the information that you get from health providers?**
  (Have the participant experienced something that can make it had to concentrate, for example an organ rejection or maybe something in his/her private life?).
- **If you have any questions on the way home today, or on the way back to the hotel, what will you do to answer those questions?**
  (Has the participant been in a situation with need for help or information?)
- **How are your family or friends concerned with information regarding life after a kidney transplant?**
- **How significant was the meeting with other kidney transplant recipients, with regard to acquiring knowledge about having a kidney transplant?**
- **[+ Other questions generated by the observation situation, like questions they had or stories they told.]**

Interview guide 2

- **How have you been since the last time we spoke? (Explore the 'trigger' concept and the hierarchy of information resources)**
  - **Have you experienced any situations where you needed information, knowledge or help? Can you tell me about that situation?**
  - **Have you experienced any situations regarding your health where you knew exactly what to do? Can you tell me about that situation?**
  - **Have you been in any situations where you were unsure what to do or where to seek information? Can you tell me about that situation?**
- **How did you experience your first consultation at your local hospital after you got home?**
  - **(Explore the feeling of contact, trustworthiness and continuity: Do they have any preferences when they search for information or help?)**
- **How was your last consultation at your local hospital?**
  - **(Explore the feeling of contact, trustworthiness and continuity: Do they have any preferences when they search for information or help?)**
- **Do you have any contact with other kidney transplant recipients?**
- **Social relations:**
  - **How does others influence the decisions that you make regarding your own health?**
    (Explore context)
- **Do you use different sources of information if you seek to answer a question?**
  - **(Explore the hierarchy of resources and different assessments regarding various information sources)**

TABLE S2: Variables associated with the nine domains of health literacy ***before*** *multiple imputation. Cells marked with yellow show where variables appear as significant or disappear as they are no longer significant*

Independent variable	**Domain 1** Supported by HCP	**Domain 2** Having sufficient information	**Domain 3** Managing health	**Domain 4** Social support	**Domain 5** Appraisal of health information	**Domain 6** Engaging with HCP	**Domain 7** Navigating	**Domain 8** Finding good health information	**Domain 9** Understanding health information
	β	*β*	*β*	*β*	*β*	*β*	*β*	*β*	*β*
5 days (ref.)									
8 weeks	.096*	.096*	.078*	-.011	.028	.069	.061	.083	.149***
6 months	.085*	.027	.022	-.097*	.010	.093*	.099*	.026	.159***
12 months	.115**	.054	-.017	-.062	.011	.111*	.075	.063	.156***
Sex (0=male 1=female)		.139**	.105*						
Age					-.007*				
Education					.153*			.173*	.224**
Civil status				.167*					
Comorbidity		-.066**		-.051*			-.059*		
Duration of kidney disease (years)	.004*					.006*	.007**	.007**	.005*
General health		.085***	.082***	.105***		.060*	.078**	.066*	
Knowledge	.045***	.026**	.018*	.027**	.025**	.042***	.043***	.032**	.029***
Self-efficacy	.023***	.027***	.017***	.018***	.018***	.032***	.034***	.031***	.034***
Number of patients (n)	**166**	**174**	**194**	**172**	**178**	**165**	**150**	**162**	**161**

TABLE S3: Variables associated with the nine domains of health literacy ***after*** *imputation. Cells marked with yellow show where variables appear as significant or disappear as they are no longer significant. Cells in green mark variables that are more significant after the imputation.*

Independent variable	**Domain 1** Supported by HCP	**Domain 2** Having sufficient information	**Domain 3** Managing health	**Domain 4** Social support	**Domain 5** Appraisal of health information	**Domain 6** Engaging with HCP	**Domain 7** Navigating	**Domain 8** Finding good health information	**Domain 9** Understanding health information
	β	*β*	*β*	*β*	*β*	*β*	*β*	*β*	*β*
5 days (ref.)									
8 weeks	.069	.121**	.077*	-.006	.039	.076	.073	.085*	.147***
6 months	.077*	.023	.019	-.109**	.018	.098*	.105*	.045	.176***
12 months	.115**	.061	-.010	-.050	.021	.132**	.113**	.079*	.176***
Sex (0=male 1=female)		.147**	.110*						
Age					-.007**				
Education								.154*	.205**
Civil status				.140*					
Comorbidity		-.058**							
Duration of kidney disease (years)	.004*						.006**	.006**	
General health	.049*	.079***	.082***	.095***		.066**	.073**	.058*	
Knowledge	.041***	.023**	.017*	.026**	.008**	.040***	.041***	.032***	.034***
Self-efficacy	.020***	.026***	.016***	.018***	.006***	.031***	.030***	.029***	.029***
Number of patients (n)	**194**	**194**	**194**	**194**	**194**	**193**	**193**	**194**	**193**

Errata for paper I

The following error was published in paper I: Patients with cytomegalovirus load of 300 copies/ml or more required treatment with antiviral medication. This should be a viral load of 600 copies/ml. The error is corrected in the thesis, and a correction has been sent to Progress in Transplantation.

Errata for the thesis

Page	Original text	Corrected text
15	In Norway, there are 28 donor-hospitals	In Norway, there are 27 donor-hospitals
21	*"Health literacy represents the cognitive and social skills which determine the motivation and promote and maintain good health."*	*"Health literacy represents the cognitive and social skills which determine the motivation and* ***ability of individuals to gain access to, understand and use information in ways which*** *promote and maintain good health."*
34	Table 4: we did not ask for postoperative complications at T4, 12 months	
47	Numbers in the table have changed places under deceased and living donor in paper I: Deceased donor: 41 (26.3%) Living donor: 115 (73.7%)	Deceased donor: 115 (73.7%) Living donor: 41 (26.3%)
44	Use of reference 156: Association GAotWM. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. The Journal of the American College of Dentists. 2014;81(3):14.	WMA DECLARATION OF HELSINKI – ETHICAL PRINCIPLES FOR MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS. World Medical Association. 2008. [Available from https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
46	The sample age was the same as in the total sample of sub-study one 56 years) and 31% were women.	The sample age was the same as in the total sample of sub-study one **(**56 years) and 31% were women.
49	..to investigate the extent to which selected sociodemographic and clinical variables, general health, self-efficacy, and transplant-related knowledge **was** associated with HL…	..to investigate the extent to which selected sociodemographic and clinical variables, general health, self-efficacy, and transplant-related knowledge **were** associated with HL…
68	Smith SG, Jackson SE, Kobayashi L, Steptoe A. Social isolation, health literacy, and mortality risk: findings from the English Longitudinal Study of Ageing. Health Psychol. 2017.	Smith SG, Jackson SE, Kobayashi L, Steptoe A. Social isolation, health literacy, and mortality risk: findings from the English Longitudinal Study of Ageing. Health Psychol. 2018;37(2):160–169.

Research

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Identifying Core Variables Associated With Health Literacy in Kidney Transplant Recipients

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Abstract

Background: A kidney transplantation requires complex self-care skills and adequate follow-up from health-care providers. Identifying strengths and limitations in different aspects of health literacy (HL) and associated variables are central to being able to improve health care. The objective of this study was to identify core variables associated with independent domains of HL 8 weeks following a kidney transplantation. **Methods:** A single-center cross-sectional study was conducted, wherein 159 kidney transplant recipients answered the Health Literacy Questionnaire (HLQ). Multivariable linear regression with backward elimination was used to investigate variables possibly associated with the 9 domains of HL. **Results:** The transplant recipients had the lowest scores in “appraisal of health information” and “navigating the healthcare system.” The highest scores were found in “feeling understood and supported by health-care providers” and “ability to actively engage with health-care provider.” General perceived self-efficacy, transplant-specific knowledge, and general health were the driving variables in several of the HL domains. **Conclusions:** The HLQ provides a more complex picture of strengths and limitations related to HL, as well as important knowledge about vulnerable groups following a kidney transplantation. The study offers an important supplement to the field of HL in kidney transplant care.

Keywords

health literacy, the health literacy questionnaire, kidney transplantation, kidney transplant recipients, multiple linear regression

Introduction

Living with a kidney transplant involves making several health-related decisions every day. The kidney transplant recipient needs to manage a complex and life-long medication regime and learn how to monitor signs of organ rejection and prevent the side effects of immunosuppressive medication. These requirements depend on the ability to find and assess relevant information, obtain knowledge, navigate the health-care system, and actively engage with health-care providers. All these attributes are closely associated with health literacy (HL), defined by the World Health Organization as “the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health.”[1(p10)]

The lack of HL capacity is associated with adverse consequences like poorer overall health and less efficient use of health services.[2] Among patients with chronic kidney disease, kidney transplant recipients seem to be a selected group, as HL correlates positively with the likelihood of being listed for and receiving a kidney transplant.[3,4] Research found that limited HL in kidney transplant recipients is associated with multiple diagnoses,[3] non-adherence to medication,[5,6] more depressive symptoms,[5] lower levels of estimated glomerular filtration rate (eGFR), and higher levels of creatinine.[5,7] Low HL is also associated with several social determinants of health: higher age,[3,8] ethnicity, lower educational level, and low income.[3,7,8] Health literacy seems to be fundamental to self-care, and

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limited HL may be a powerful risk factor following kidney transplantation.

Most studies that assess HL use measures that reflect only a few of the aspects that are covered by well-known definitions of HL.[9] In the existing literature, assessments are often dominated by the Rapid Estimate of Adult Literacy in Medicine, the Test of Functional Health Literacy in Adults, or measurements based on these.[9,10] These questionnaires are designed to assess word recognition, reading comprehension and numeracy, and have contributed fundamentally to the development and implementation of educational materials and oral instructions. Patient experiences related to navigating the health-care system, communicating with health-care professionals, and experiencing social support in everyday life constitutes a knowledge gap. Identifying a broader range of aspects and exploring the complexity of HL may provide valuable knowledge in a clinical setting and may be vital to the continuous development of health-care services.

The present study was conducted in a Norwegian setting where 1 national transplant center serves the whole population. After 8 weeks of close follow-up and individual patient education,[11] follow-ups are transferred to local hospitals and recipients are left with increased responsibility for self-care. It would be of clinical importance to gain knowledge about factors that are associated with HL prior to transfer to be able to identify vulnerable groups and support self-care behavior.

The objective of this study was to identify core variables related to different aspects of HL and to gain more detailed and comprehensive knowledge of HL. Our research question was the following: what is the importance of selected sociodemographic and clinical variables, self-reported health, transplant-related knowledge, and self-efficacy to each of the domains of HL as measured by the Health Literacy Questionnaire (HLQ) at 8 weeks after kidney transplantation?

Materials and Methods

This single-center cross-sectional study was part of a larger prospective study that aimed to investigate HL and transplant-related quality of life during the first year following a kidney transplantation. The research project was approved by the Norwegian Regional Ethical committee (#2016/1485) and the data protection officer at the hospital (#2016/14592). The study was conducted according to the Declaration of Helsinki. All invited patients were given oral and written information, and participants gave written informed consent before inclusion.

Setting and Population

The study took place at the Norwegian national transplant center, where all transplant surgery is conducted. Between 250 and 300 kidney transplantations are done annually at the center and about 25% of the kidney grafts come from a living donor. The study was conducted from February 2016 to August 2017. During this period, 357 patients received a kidney transplant. Nurses trained to provide the informed consent invited potential participants at the surgical ward, 3 to 5 days posttransplantation. The questionnaire was handed out by a nurse during the last consultation at the outpatient ward at 8 weeks following the transplantation. The participants filled out the questionnaire at the hospital on the same day. No remuneration was given for participation.

Criteria for inclusion in the study were being 18 years or older, not being isolated due to contagious diseases, being able to participate in patient education post-transplantation, and know Norwegian well enough to fill in the questionnaire.

Measures

Health Literacy Questionnaire

Health literacy was measured by the multidimensional HLQ.[12] The questionnaire contains 44 questions across 9 independent domains, each of which contains 4 to 6 questions.[12] In the first 5 domains, respondents were asked to select 1 of 4 responses to a statement: “strongly disagree,” “disagree,” “agree,” or “strongly agree.” The last 4 domains asked about capability and respondents selected 1 of 5 responses: “cannot do or always difficult,” “usually difficult,” “sometimes difficult,” “usually easy,” or “very easy.” The questionnaire does not have a total score, but a mean domain-specific score, calculated by adding each of the answers in a domain and dividing the score by the number of items in the specific domain. The calculations were carried out using the IBM SPSS Statistics version 25 (IBM Corp, Armonk, New York) scoring algorithm that followed the user manual from the developers of the HLQ. A higher score indicated higher HL.

The questionnaire has been shown to have strong construct validity and reliability and has high acceptability to clients and clinicians.[12] The HLQ has been translated and adapted for the Norwegian language according to the principles of translation developed by the instrument authors.[13]

Transplantation Knowledge Questionnaire

Knowledge was measured by the Knowledge Questionnaire for Renal Recipients.[14] The questionnaire was developed and validated in a Norwegian setting and focuses on medication, rejection symptoms, and lifestyle.[14] The questionnaire was considered to be the best available instrument since it was developed to capture specific transplant-related knowledge relevant to the Norwegian patient education program.[11] Due to changes in patient education since the questionnaire was first used in 2007 to 2009,[14] 5 questions were no longer relevant and were excluded by the developers of the questionnaire (items 8, 9, 12, 15, and 17). The revised questionnaire contains 14 statements which were rated using a 5-point scale anchored from the left with the wording “totally disagree” to “totally agree.” When scoring the questionnaire, only completely correct answers (1 or 5) were given points, and a total score of the correct answers was summarized. Answers in the middle were interpreted as insecurity and were not given points. Some of the items were reverse coded so that each item was scored to reflect the degree of correctness. The questionnaire gave a total score from 0 to 14, with higher scores indicating a higher level of knowledge.[14]

General Perceived Self-Efficacy Scale

The General Perceived Self-Efficacy (GSE) scale was used to assess self-efficacy, which refers to the self-perceived ability to cope with various challenges.[15] The questionnaire contains 10 statements concerning an individual's belief in their ability to respond to novel or difficult situations. Each statement has a 4-point response scale from "not at all true" to "exactly true" (ranging from 1-4). The scores for each item give a total GSE score between 10 and 40 points, with a higher score indicating higher self-efficacy (Cronbach α for current data was .90).

General Health, Single Item

We used a single item to assess the self-perceived evaluation of general health.[16] This question was, "In general how would you say your health is?," with the 5 response categories "excellent," "very good," "good," "fair," or "poor." A higher score indicates poorer general health (range 1-5). The scores were reverse coded, such that a higher score represents a higher level of general health in the regression analysis.

Sociodemographic and Clinical Factors

Information regarding the length of kidney disease, previous kidney transplantations, and donor status were collected with the questionnaire. From the electronic health record, we obtained information about the dialysis status before the transplantation, blood test results 8 weeks post-transplantation, postoperative complications, infections, rejections, and other diseases. We used the Charlson Comorbidity Index[17] to calculate comorbidity.

Surgical complications were defined as complications calling for interventions. Postoperative infections were defined as infections requiring active treatment. Cytomegalovirus was registered if the participants had a viral load of 300 copies/mL or more, which requires treatment in Norwegian transplant follow-up protocol.

Statistical Analysis

Data analysis was done using IBM SPSS Statistics version 25 (IBM Corp, Armonk, New York). Missing data in the HLQ were handled using the expectation–maximization algorithm, following the HLQ user manual. Scales with 4 to 5 questions allowed for 2 missing values to be imputed. Scales with 6 questions allowed for 3 missing values to be imputed. The knowledge questionnaire allowed for 2 missing items. Missing items were given the score 0. The GSE allowed for 3 missing items. Total score was found by calculating the mean score. Mean and standard deviation, median, and range were used to describe the sample and the variables included in the analysis. Cronbach α was calculated to assess the internal consistency of the HLQ and the GSE scale.

Multivariable linear regression with backward elimination was used to determine variation in HL. We used a purposeful selection approach to decide which variables to include in the regression models, involving 3 steps:

Univariable linear regressions were performed with each of the 9 HL domains as dependent variables and all possible covariates were tested individually. The variables with a P value of <.20 in univariable analysis were selected for inclusion in the first multivariable model.

Backward elimination involved removing the variable with the highest P value and repeating the regression analysis until all variables had a significance level of <5%.

Finally, variables with a significance level of $\geq .20$ in the univariable analysis were reincluded to see whether they became statistically significant in each of the 9 regression models.

Assumptions of normality, linearity, multicollinearity, and homoscedasticity were met in all 9 regression models. To be able to compare the importance of each variable in the regression models, the standardized β coefficients (std β) are provided. The adjusted R^2 is given to describe how much of the variation in HL is explained by the model.

Result

Descriptive Data

During the inclusion period, 217 patients were invited to participate in the current study, and 199 patients accepted the invitation. After 8 weeks, 159 participants answered the questionnaire and, of these, 143 participants gave consent to the retrieval of clinical data (Figure 1).

The mean age of the participants was 56 years (standard deviation [SD] 13.7), ranging from 20 to 81, and 31.4% of the participants were women (Table 1). Fifty-nine (41.3%) participants were transplanted preemptively, while 84 (58.7%) participants were in dialysis before the transplantation. Twenty-five (16.1%) participants had undergone kidney transplantation earlier, and 41 (26.3%) participants received a kidney from a living donor.

Five participants had missing data in 1 or more of the HLQ scales after imputation. Three participants had 1 missing item in the knowledge questionnaire and 1 participant had 1 missing item in the GSE. The calculation of Charlson Comorbidity Index did not include age, since the Charlson score with age had high collinearity with age in the regression analyses.

The 9 domains of the HLQ were normally distributed. The mean scores and Cronbach α are shown in Table 2. In the first 5 scales (ranging from 1-4), the highest score was found in "feeling supported by health-care providers" (3.43, SD: 0.49), while the "appraisal of health information," had the lowest score (2.81, SD: 0.56). Among the last 4 domains (ranging from 1-5), the lowest score was found in "navigating" (3.8, SD:

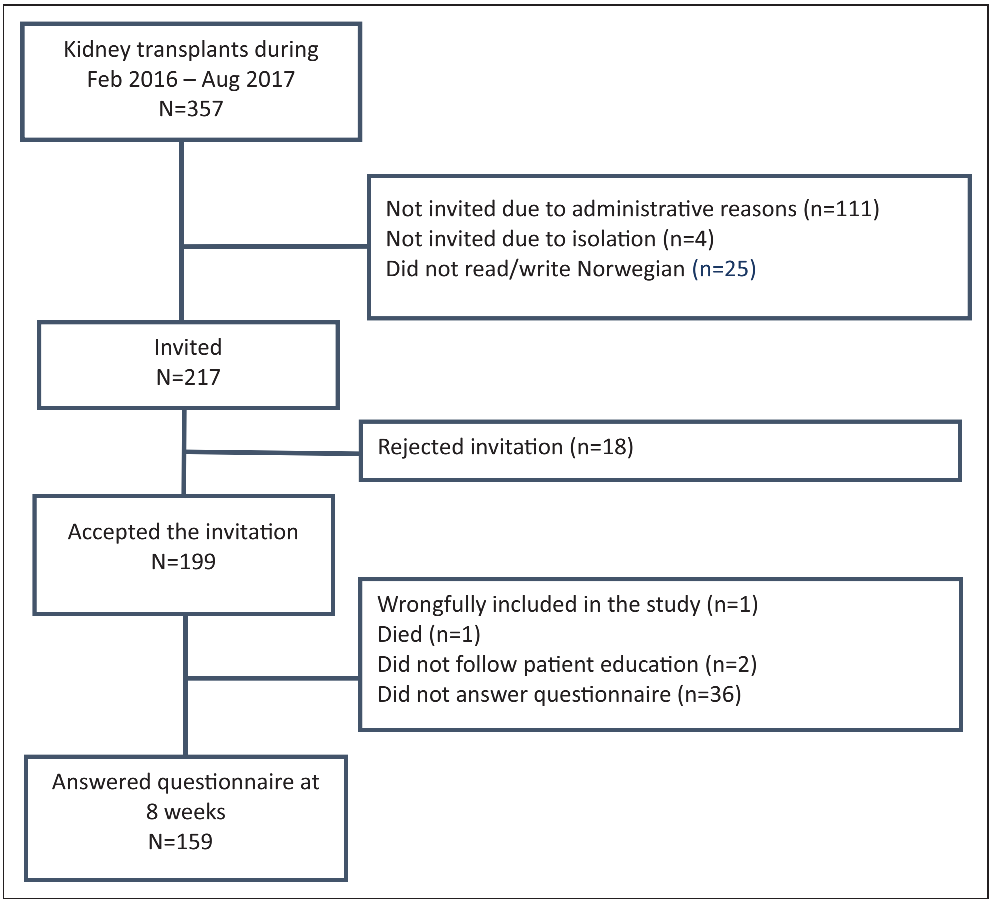

Figure 1. Flow diagram of study participants.

0.56), and the highest score was found in "engaging with health-care providers" (4.13, SD: 0.54).

Eighteen of 24 variables had a *P* value <.20 and were included in the first regression models for 1 or more of the 9 HL domains. None of the remaining 6 variables became significant when reincluded in the final regression models (Table 3).

Regression Analysis

The results of the final regression models are shown in Table 4. In "feeling supported by health-care providers," the model explained 15% of the variability. Higher scores in the first domain were found in younger participants and participants with higher score in transplant-related knowledge and higher self-efficacy. More knowledge was the most important variable in the model with std β of .28. This means that every time the knowledge score increases by 1 SD, the score in "feeling supported by health-care providers" increases by 0.28 SD, when all other variables are constant.

In "having sufficient information," lower age, better general health, higher knowledge scores, and higher self-efficacy were associated with higher scores. The model explained 26% of the variability, and self-efficacy was the driving variable with std β of .34.

In "managing my health," the model explained 17% of the variance. Participants with a kidney from a deceased donor, peritoneal dialysis pretransplantation, better general health, and higher self-efficacy had higher scores. The importance of each variable was quite similar, but the highest std β was found in self-efficacy and peritoneal dialysis (std β = .20).

In "social support," the model explained 9% of the variance and included 2 variables; general health and knowledge. General health was the driving variable in the model with std β of .26.

In "appraisal of health information," the model explained only 2% of the variance, with age as the only significant variable (std β of −.17).

The R^2 in "engaging with health-care providers," indicates that the model explained 33% of the variance. Longer duration of kidney disease, better general health, more knowledge, and higher self-efficacy were associated with higher HL scores. Self-efficacy had the largest std β of .38.

In "navigating," longer duration of kidney disease, experiencing postoperative infections, better general health, more knowledge, and higher self-efficacy was associated with higher HL scores and explained 29% of the variance. Also in this model, self-efficacy was the driving variable with std β of .34.

The regression model in "finding good health information" explained 38% of the variance and included the duration of

Table 1. Sample Characteristics of Kidney Transplant Recipients.

Variables	N	N (%)	Mean (SD)	Median (Min-Max)
Age at the time of transplantation (years)	159		56.1 (13.7)	58 (20-81)
Sex	159			
Women		50 (31.4)		
Men		109 (68.6)		
Civil status	153			
Married/living with a partner		111 (72.5)		
Single/divorced/separated/widow(er)		42 (27.5)		
Education	143			
Completed lower education		78 (54.5)		
Higher education		65 (45.5)		
Work status before transplantation	154			
Working		57 (37.0)		
Not working (disabled/retired/student/unemployed/other)		97 (63.0)		
Ethnicity	159			
Norwegian		147 (92.5)		
Non-Norwegian		12 (7.5)		
Duration of kidney disease (years)	136		16.7 (14)	11 (1-55)
History of earlier transplantations	155			
First time		130 (83.9)		
Being transplanted before		25 (16.1)		
Donor status	156			
Living donor		41 (26.3)		
Deceased donor		115 (73.7)		
Number of comorbidities	143		1.2 (1.3)	1 (0-6)
Status of dialysis before transplantation	143			
Preemptive dialysis		59 (41.3)		
Peritoneal dialysis		26 (18.1)		
Hemodialysis		58 (40.6)		
Months in dialysis	85		18.5 (13.3)	17 (0-74)
Blood samples 8 weeks posttransplantation				
Creatinine (μmol/L)	142		135.1 (66.5)	122.5 (47-782)
Estimated glomerular filtration rate (mL/min/1.73 m^2)	142		52.8 (15.5)	50 (14-106)
Tacrolimus concentration (μg/L)	139		6.5 (1.8)	6.2 (1.4-15.5)
Complications following transplantation				
Organ rejection	141	19 (13.5)		
Surgical complications	142	20 (14.1)		
Infections	142	28 (19.7)		
Cytomegalovirus	142	26 (18.3)		
General health score (scale range 1-5)	157		3.4 (0.9)	3 (1-5)
Total knowledge score (scale range 0-14)	158		10.3 (2.6)	11 (0-14)
Total self-efficacy score (scale range 10-40)	155		32.5 (4.6)	33 (22-40)

Abbreviation: SD, standard deviation.

kidney disease, history of earlier transplantations, peritoneal dialysis, general health, knowledge, and self-efficacy. General health had the largest std β of .31.

In the last domain, "understanding health information," higher level of education, history of earlier transplantations, peritoneal dialysis before the transplantation, better general health, higher knowledge, and better self-efficacy correlated with higher scores and explained 29% of the variance. Knowledge was the most important variable in the model (std $\beta = .29$).

Discussion

In the present study, HL was assessed 8 weeks post-transplantation. Overall, the mean scores of the HLQ were above the critical low scores of $\leq$2.0 in domains 1 to 5, which involves the shift from "disagree" to "agree," and $\leq$3.0 in domains 6 to 9, involving moving from "sometimes difficult" to "usually easy." In the first 5 domains, the models explained 2% to 26% of the variance in HL. In the last 4 domains, the models explained between 29% and 38% of the variance. Self-efficacy, transplantation-specific knowledge, and general health were identified as core variables. Sociodemographic and clinical factors had lower std β overall and were less significant in the regression models.

Domain 5, "appraisal of health information," stands out as the most challenging of the 9 domains. Demian et al[5] had a similar finding in their Canadian study of kidney transplant recipients, and Stømer et al[18] found the same pattern among

Table 2. Dimensions in the Health Literacy Questionnaire.[a]

Health Literacy Domains *Short Form*	Number of Items	Range	N	Mean (SD)	95% Confidence Interval	Cronbach α
1. Feeling understood and supported by health-care providers *Feeling supported by health-care providers*	4	1-4	158	3.43 (0.49)	3.35-3.51	.84
2. Having sufficient information to manage my health *Having sufficient information*	4	1-4	156	3.27 (0.46)	3.20-3.35	.80
3. Actively managing my health *Managing my health*	5	1-4	157	3.23 (0.44)	3.16-3.30	.84
4. Social support for health *Social support*	5	1-4	157	3.22 (0.46)	3.15-3.29	.76
5. Appraisal of health information *Appraisal of health information*	5	1-4	157	2.81 (0.56)	2.72-2.89	.77
6. Ability to actively engage with health-care providers *Engaging with health-care providers*	5	1-5	155	4.13 (0.54)	4.04-4.21	.86
7. Navigating the health-care system *Navigating*	6	1-5	155	3.80 (0.56)	3.72-3.90	.86
8. Ability to find good health information *Finding good health information*	5	1-5	155	3.83 (0.56)	3.75-3.92	.82
9. Understand health information well enough to know what to do *Understanding health information*	5	1-5	155	4.01 (0.53)	3.92-4.10	.80

Abbreviation: SD, standard deviation.

[a] Higher scores indicate better health literacy. Domains 1 to 5 have the answering options (1) strongly disagree, (2) disagree, (3) agree, and (4) strongly agree. Domains 6 to 9 have the answering options (1) cannot do or always difficult, (2) usually difficult, (3) sometimes difficult, (4) usually easy, and (5) very easy.

Norwegian patients with chronic kidney disease. One reason for this finding might be that critical appraisal of health information has little focus on patient education. However, statements related to this domain assume a critical analysis of all information, which respondents might not feel is necessary in cases where most information comes from health-care providers and experts in the field.

To the best of our knowledge, there are no other studies that have investigated the association between HL and self-efficacy in kidney transplant recipients. Self-efficacy contributed in 7 of 9 domains of HL and was the driving factor in "having sufficient information," "managing my health," "engaging with health-care providers," and "navigating." Self-efficacy involves a self-confident and optimistic view of one's ability to cope with life stressors.[15] Higher self-efficacy in kidney transplant recipients is associated with better self-care management,[19] and health-related behaviors such as adherence.[20] Nutbeam[21] emphasizes that improving HL requires a focus on developing not only age- and context-specific health knowledge but also the self-efficacy necessary to put knowledge into practice. Beliefs about efficacy affect both motivation and action[19,20] and may therefore be a crucial link in understanding the processes inherent in the concept of HL.

Transplant-specific knowledge was important in explaining the variance in 7 of the 9 regression models and was the driving factor in "feeling supported by health-care providers" and "understanding health information." Baker[22] states that while knowledge does not in itself constitute HL, conceptual or disease-specific knowledge is a resource that facilitates HL.[22] It is also possible to see this the other way around, namely that HL involves the capacity to acquire new knowledge. One important finding was the association between knowledge and the domains that involved interaction with health-care providers. Participants with more knowledge had higher scores in "feeling supported by healthcare providers" and "engaging with healthcare providers." There may be several explanations for these results. It is possible that both nurses and doctors overestimate patients' HL.[23,24] This could make health-care personnel less sensitive towards HL needs and challenges. Easton et al[25] found that patients with low HL had problems understanding the language of the clinical staff and were afraid to admit that they did not understand. Shame and fear of stigma could make patients distance themselves from health-care providers.[25] Health-care providers thus need to be aware that a lack of knowledge may impede good communication. Indeed, Edwards et al[26] emphasize the role of the health-care provider, as they can either empower patients and facilitate HL or disempower them and limit HL.

General health was also important in explaining the variance in 7 of the 9 HL domains and was the driving variable in "finding good health information" and "social support." It may be that perceived poor general health is connected to a lower capacity to find and use health information or navigate the health-care system. However, reduced health may also increase the need for information, thereby making it harder to find sufficient information of good quality. Social support has been found to have a fundamental influence on HL.[27,28] Family and friends can act as surrogate decision makers or seek health care on behalf of the patient.[28] Along these lines, the term distributed literacy[27] can help us understand HL as a social process,

Table 3. Univariable Linear Regression Models.[a]

Variables	Domain 1 Feeling Supported by Health-Care Providers	Domain 2 Having Sufficient Information	Domain 3 Managing My Health	Domain 4 Social Support	Domain 5 Appraisal of Health Information	Domain 6 Engaging With Health-Care Providers	Domain 7 Navigating	Domain 8 Finding Good Health Information	Domain 9 Understanding Health Information
Standardized β coefficient	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β
Age at the time of transplantation	**−.168**	**−.220**	−.052	−.102	**−.173**	−.048	−.042	**−.176**	−.092
Sex (0 = man, 1 = woman)	.063	.071	**.107**	−.003	−.011	**.122**	**.134**	.058	.090
Civil status (0 = married/partner, 1 = divorced/ widowed/ alone)	**−.128**	.000	.018	**−.110**	.046	−.085	−.046	−.084	**−.121**
Education (0 = primary and secondary school, 1 = higher education)	**.154**	.088	.005	.001	.079	**.114**	.085	**.203**	**.254**
Work status before transplantation (0 = working, 1 = not working)	.078	**.164**	−.001	**.170**	**.106**	.097	.050	**.162**	**.181**
Ethnicity (0 = Norwegian, 1 = non-Norwegian)	−.070	.051	−.030	.007	.021	.028	−.084	.055	.013
Duration of kidney disease (years)	**.160**	.091	.107	**.172**	**.120**	**.244**	**.295**	**.240**	**.177**
History of previous transplantations (0 = no, 1 = yes)	**.186**	**.105**	−.031	.067	**.137**	**.174**	.095	**.208**	**.168**
Donor status (0 = living, 1 = deceased)	.003	.028	**.232**	.032	.086	.094	.056	.039	−.040
Number of comorbidities	**−.139**	**−.201**	−.033	**−.175**	−.079	−.104	**−.152**	−.105	−.027
Preemptive dialysis (0 = HD or PD, 1 = not in dialysis)	−.002	.056	.013	.095	−.043	.030	.098	.059	.058
PD (0 HD or not in dialysis, 1 = PD)	.096	**.117**	**.231**	**.125**	**.117**	**.130**	.075	**.204**	**.148**
HD (0= not in dialysis or PD, 1 = HD)	−.073	**−.149**	**−.196**	**−.194**	−.049	**−.134**	**−.159**	−.103	**−.177**
Months in dialysis	−.051	−.095	−.087	−.097	−.012	**−.152**	−.104	−.080	**−.227**
Creatinine	.076	.047	.115	.052	.121	.095	.065	.034	.026
Estimated glomerular filtration rate	.104	.068	.028	.079	.063	.010	−.006	**.128**	.079
Tacrolimus concentration	.018	−.051	−.014	.009	.048	−.024	−.069	.083	.023
Organ rejection (0 = no, 1 = yes)	.012	.009	−.065	.087	−.032	−.029	−.014	−.050	.009
Surgical complications (0 = no, 1 = yes)	−.002	.010	−.017	.018	.011	−.051	.072	**−.121**	−.071
Infections (0 = no, 1 = yes)	.053	.033	.060	.032	.054	.077	**.187**	.106	.098
Cytomegalovirus (0 = no, 1 = yes)	−.026	−.035	−.003	−.036	−.021	−.052	−.086	−.069	−.014
General health score (higher score—better health)	**.106**	**.299**	**.266**	**.228**	**.118**	**.259**	**.196**	**.327**	**.251**
Knowledge (higher score—more knowledge)	**.302**	**.187**	**.184**	**.187**	**.145**	**.307**	**.269**	**.254**	**.307**
Self-efficacy (higher score—better self-efficacy)	**.233**	**.405**	**.261**	**.170**	**.141**	**.440**	**.390**	**.374**	**.364**

Abbreviations: HD, hemodialysis; PD, peritoneal dialysis.

[a] Association between selected variables and the 9 domains of HL are described with standardized β coefficients. Coefficients in bold had a *P* value <.2 in univariable analysis and were included in the multivariable regression models.

Table 4. Linear Regression Models Explaining Variance in the 9 Domains of the Health Literacy Questionnaire.

Variables	Domain 1 Feeling Supported by Health-Care Providers	Domain 2 Having Sufficient Information	Domain 3 Managing My Health	Domain 4 Social Support	Domain 5 Appraisal of Health Information	Domain 6 Engaging With Health-Care Providers	Domain 7 Navigating	Domain 8 Finding Good Health Information	Domain 9 Understanding Health Information
Total N[a]	152	149	136	154	157	127	114	115	120
Standardized β coefficient	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β	Std. β
Age at transplantation	−.16 ($P = .042$)	−.17 ($P = .021$)			−.17 ($P = .030$)				
Education									.19 ($P = .017$)
Duration of kidney disease						.18 ($P = .015$)	.22 ($P = .009$)	.18 ($P = .024$)	
History of earlier transplantations								.20 ($P = .010$)	.18 ($P = .026$)
Donor status			.18 ($P = .024$)						
Peritoneal dialysis prior to transplantation			.20 ($P = .012$)					.21 ($P = .006$)	.16 ($P = .043$)
Postoperative infections							.17 ($P = .039$)		
General health score		.21 ($P = .006$)	.19 ($P = .019$)	.26 ($P = .001$)		.15 ($P = .047$)	.17 ($P = .045$)	.31 ($P < .001$)	.23 ($P = .005$)
Total knowledge score	.28 ($P < .001$)	.17 ($P = .018$)		.19 ($P = .016$)		.28 ($P < .001$)	.19 ($P = .020$)	.21 ($P = .007$)	.29 ($P < .001$)
Total self-efficacy score	.20 ($P = .009$)	.34 ($P < .001$)	.20 ($P = .015$)			.38 ($P < .001$)	.34 ($P < .001$)	.26 ($P = .001$)	.21 ($P = .011$)
Adjusted *R*2	**.15 ($P < .001$)**	**.26 ($P < .001$)**	**.17 ($P < .001$)**	**.09 ($P < .001$)**	**.02 ($P = .030$)**	**.33 ($P < .001$)**	**.29 ($P < .001$)**	**.38 ($P < .001$)**	**.29 ($P < .001$)**

[a] N change in the different models depending on which variables are included.

where people with different strengths and limitations can support each other and become more fully literate individuals.[27] It may be helpful to identify social support in a clinical setting since patients with little support may depend more on a closer relationship with their health-care providers.

Duration of kidney disease, history of earlier transplantation, and postoperative infections may all be considered as variables reflecting experience-based knowledge. Edwards et al[26] found that knowledge and HL skills increased in patients with long-term health conditions and argue that HL is generative and changes over time. These findings support the assumption that skills facilitating HL may improve with time and experience.

Previous studies have found a positive association between HL and receiving a kidney from a living donor.[3,8,29] However, we did not find this to be the case in our study. On the contrary, we found a small association between receiving kidney from a deceased donor and "managing my health." Having been in peritoneal dialysis before the transplantation also seemed to be associated with some aspects of HL. However, these participants also had higher education in our data, and we have reason to believe that patients in peritoneal dialysis are a selected group who are rather resourceful. Demian et al[5] found a positive association between lower levels of creatinine and "appraisal of health information." Also, higher eGFR was associated with "understanding health information."[5] However, none of these clinical variables became significant in any of our models.

Health literacy is about understanding the interaction between the demands of the health-care system and the abilities of an individual. To be able to meet patient needs, it is an important task for health-care providers to identify risk factors for HL. This study has shown that self-efficacy, transplant-specific knowledge, and general health are key variables in explaining variance in several aspects of HL. The results provide essential knowledge about which patients may need extra attention in the time before and after discharge 8 weeks posttransplantation.

Strength and Weaknesses

The HLQ is subjective and gave information about patient experiences. However, we have no information about objective measures of HL, and it is not possible to address whether respondents overestimated their own HL skills.

Due to the number of regression analyses and of P values, we cannot exclude the possibility of false-positive findings. Hence, we have focused on results with P value <.01 in the results and in the discussion.

Twenty-five patients did not read and understand Norwegian well enough to answer the questionnaire. We know from other studies that language barriers are associated with lower HL scores.[2,5] We did not find any association between limited HL and being non-Norwegian, but these participants also spoke Norwegian well enough to be included in the study.

For administrative reasons, 111 patients were not invited to participate in the study—these comprise 31% of the transplanted population in the period of inclusion. We did not have permission to gather information about the patients that were not invited. We, therefore, do not know if they deviate from the study population, only that our selection process was random and not systematic.

This cross-sectional study only gives us a snapshot of the strengths and limitations of HL 8 weeks posttransplantation. However, measures of HL might be artificially high since the participants were close to health-care providers the whole time. We need more knowledge about how HL might develop over time to see if these are relatively stable or changeable traits following a kidney transplantation.

Conclusion

Using the multidimensional HLQ, we have captured strengths and limitations in various aspects of HL. Having 1 score for every dimension enabled us to differentiate between what respondents found easy and what was more challenging. The study provides a more complex picture of HL in the context of kidney transplant recipients and offers an important supplement to the field of HL in kidney transplant care.

Authors' Note

K.G.D., M.H.A., K.H.U., E.E., and A.K.W. have contributed to the planning of the study and the study design. K.G.D. and M.H.A. organized the data collection at the transplant surgery ward and the outpatient ward. K.G.D. conducted the statistical analysis together with statistician R.S.F., and in continuous discussions with M.H.A., K.H.U., E.E., and A.K.W. All authors have contributed to the process of drafting the results of the study and completing the article.

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PLOS ONE

RESEARCH ARTICLE

The trigger-information-response model: Exploring health literacy during the first six months following a kidney transplantation

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Abstract

The main objective of this study was to explore how kidney transplant recipients find, understand, and use health information, and make decisions about their health—also known as health literacy. Kidney transplant recipients must take an active part in their health following the transplantation, since a new organ requires new medication and focus on lifestyle to prevent side-effects and signs of organ rejection. Consequently, it is of major clinical relevance to explore how kidney transplant recipients understand and relate to health literacy. Ten kidney transplant recipients were interviewed at three weeks and again at six months post-transplantation. Design and analysis were inspired by constructivist grounded theory. The results of the study are presented through a model consisting of three phases: the trigger phase, the information phase, and the response phase. The participants were influenced by context and personal factors as they moved between three phases, as information seekers, recipients, and sharers. This study illustrates health literacy as an active process. It gives new insight into what motivates kidney recipients to find, share, and receive information, and how a hierarchy of resources is built and used.

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Data Availability Statement: Due to Norwegian ethical guidelines, we are not able to make our data public. Our data material comprise transcribed interviews from a small patient population and public access will compromise patient confidentiality and privacy. However, we may provide four interviews with key informants that are processed and de-identified, to protect the confidentiality and privacy of the participants. These interviews will constitute as our minimal data set. They will be translated to English and be

Introduction

Health literacy as a concept has developed over the past three decades, initially focusing on reading and numeracy skills and now covering much broader competencies. The World Health Organization [1] defines health literacy as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health". They further state that "health literacy implies the achievement of a level of knowledge, personal skills, and confidence to take action to improve personal and community health by changing personal lifestyle and living

available on request. The request may be addressed to the surgeon and research manager at the Section of Transplant Surgery, Oslo University Hospital, Einar Martin Aandahl. He may be reached at the following e-mail: einar.martin.aandahl@ous-hf.no.

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conditions". Thus, health literacy brings together different concepts related to what people need in order to make good decisions about their health [2].

Today we know that limited health literacy is associated with numerous negative consequences, both in the general population [3] and also for patients with chronic conditions [2, 4]. Kidney transplant recipients often have a long history of chronic renal disease and comorbidities. Following a transplantation, the recipients depend on lifelong immunosuppressive medication to avoid rejection of the new organ. At the same time, the transplant recipients must be aware of their health in order to monitor signs of rejection and reduce the extent of adverse effects such as infections [5], cardiovascular disease [6], osteoporosis and skin cancer [7, 8]. The available literature on health literacy in kidney transplant recipients is exclusively quantitative, measuring health literacy with generic [9–15] and transplant-specific tools [9, 14, 16]. Studies indicate that kidney transplant recipients constitute a selected group, as the level of health literacy seems to be higher for patients who are awaiting or have already received a kidney transplant compared to other patients with chronic kidney disease [10, 16–19]. However, we do know that limited health literacy in kidney transplant recipients is associated with non-adherence to medication [12, 20], higher creatinine level [14], and comorbidity [18]. Findings also imply an association between low health literacy and lower socioeconomic status [14, 15], lower educational level [13, 14, 19], unemployment, and long-term disability [18].

Existing studies have contributed to our knowledge of health literacy in the context of kidney transplant recipients, yet we call for a deeper understanding of what constitutes health literacy when applied in real-life situations. Further insight into how kidney transplant recipients understand and address health information and make decisions about their own health would have major clinical relevance in patient follow-up. This article takes a bottom-up approach to health literacy. Rather than taking the concept for granted we explore how "health literacy" makes sense from a transplant recipient's point of view. Through the use of semi-structured interviews and observing interactions with healthcare providers, we focus on the first six months following the transplantation. In this early stage, requirements for adaptation and health literacy skills are challenged, and it is crucial to evolve follow-up programs and initiate interventions of good quality and clinical relevance.

Methods

Context

Norway has one nationwide transplantation center where all kidney transplantations are performed and where recipients are followed closely during the first eight postoperative weeks. Recipients remain on the surgical ward for one week before being transferred to the outpatient ward. Patients living close to the hospital can stay at home during this period, while others must stay at the patient hotel. After discharge, a local kidney specialist (nephrologist) follows up with the kidney recipients. All kidney transplant recipients undergo comprehensive, individual patient education starting the first week on the surgical ward, followed by three sessions on the outpatient ward [21].

Designing the study

In the present study, we chose a qualitative design using semi-structured interviews to explore health literacy in an inductive and situated way. Participatory observations were used to prepare for the first round of interviews. Existing multidimensional definitions of health literacy partially guided the thematic focus concerning both interviews and observations. However, we also sought to move beyond the current, dominant definitions and explore aspects not captured by these. This meant that the participants' subjective understandings were analyzed as equally plausible and valuable constructions of the world. The study design and analysis were inspired by constructivist grounded theory [22], which follows the inductive, emergent, open-ended, and iterative approach of Glaser and Strauss, but treats data and theorizing as constructed, not discovered [23].

Patient involvement

A user representative from the National Association for Kidney Patients and Transplant Recipients was involved in the planning and completion of the study. The patient adviser was invited to comment on the interview guide, the analysis of the interviews, and the writing of the article, to ensure that the content was understandable and to discuss whether the findings were recognizable to him as a transplant recipient.

Sample

Ten kidney transplant recipients were asked to participate in the study by a nurse on the surgical or outpatient ward, approximately 6–10 days post-transplantation. All of the patients accepted the invitation. Since the aim was to capture a wide range of perspectives concerning health literacy, we used purposive sampling to achieve maximum variation (Table 1). The participants came from different areas of Norway and had different socioeconomic and sociodemographic backgrounds as well as different diagnoses. The participants were already part of a larger quantitative study in which they had answered the multidimensional Health Literacy Questionnaire [24] five days post-transplantation. Scores from this instrument were used as selection criteria to invite participants reporting various health literacy challenges and strengths (S1 Table).

Data collection

In the process of planning the interviews and the interview guide, we observed the participants in two different consultations with healthcare personnel: one consultation with a nephrologist approximately 7–10 days post-transplantation; and the second at three weeks post-transplantation, in the form of individual patient education with a nurse (Table 2). Communication with healthcare providers is an important aspect of health literacy, and the observations functioned as a relevant basis for asking questions about how the participants experienced interacting with healthcare providers, receiving, evaluating, and asking for relevant information. The interview guide (S2 Table) functioned as a basis for the interview, helping to relate health literacy to specific experiences. However, other reflections and experiences relevant to health literacy were also pursued.

The combination of observation and interview was pilot-tested in a clinical setting before data gathering commenced. KGD undertook the participatory observations and was introduced to the participants as both a researcher and a transplantation specialist nurse. The first round of interviews was conducted three weeks post-transplantation by KGD and MHA; MHA was introduced as a researcher at the transplant clinic. KGD conducted the second round of interviews six months post-transplantation (Table 2). The second round of interviews was inspired by life-form interviews [25], which explicitly focus on experiences in everyday life. The questions were more open-ended than in the first round and were concentrated around how health literacy was applied in real-life situations. The interview guide in this round also contained major themes from the first round, further exploring the concept of triggers, contact, trustworthiness, and continuity, and how this influenced the creation of a possible hierarchy of information resources (S2 Table). Before each interview, the participants were introduced to the term "health literacy" as follows: "health literacy involves how you seek,

Table 1. Sample description.

Age		28–78 years
Sex	Women	5
	Men	5
Duration of kidney disease		2–38 years
Living at home during first interview		3
Living at patient hotel during first interview		7
Dialysis status pre transplantation	Pre-emptive dialysis	4
	Peritoneal dialysis	2
	Hemodialysis	4
Donor status	Deceased donor	7
	Living donor	3
Transplantation status	First time	9
	Second time	1
Civil status	Living alone	3
	Living with a partner	7
Ethnicity	Norwegian	9
	Non-Norwegian	1
Level of education	Completed primary and lower secondary school	1
	Completed upper secondary and/ or vocational school	4
	Less than four years of higher education	4
	More than four years of higher education	1
Employment status	Working at time of transplantation	4
	Homemaker	1
	Student	1
	Retired	2
	Disability pension	2
Diagnosis	Nephrosclerosis	
	Congenital multiple malformations	
	Secondary amyloidosis	
	Glomerulonephritis	
	Diabetic nephropathy	
	Lupus nephritis	
	Recurrent pyelonephritis	
	Alport syndrome	
	Polycystic kidney disease	

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understand, and use the information that you feel you need to take care of your health; health literacy is about the social support you have around you, how you experience interaction with healthcare personnel and your experiences of navigating the healthcare system; and finally, health literacy is about the different decisions you make that may influence your health".

Analysis

The observations were only used to generate questions for the first interviews and were not analyzed further. KGD and an assistant transcribed the interviews. The transcripts were not returned to the participants. KGD undertook the coding, in continuous discussion with the co-authors and with use of NVivo 11. The transcribed material was coded line-by-line, followed by focused coding and theoretical categorizations (Table 3) [22]. Line by line coding

Table 2. Overview of data collection.

	Duration	Recordings and notes	Location/ context	Time	Focus
First observation: generating questions for first interview	13–35 minutes	Audio recording Field notes and questions for the first interview	One of the first consultations with a nephrologist on the outpatient ward	8–14 days post-transplantation	Observation guide: non-verbal communication, atmosphere and potential questions for interview
Second observation: generating questions for fist interview	25–45 minutes	Audio recording Field notes and questions for the first interview	The second individual patient education session on the outpatient ward with a nurse	Three weeks post-transplantation	Observation guide: non-verbal communication, atmosphere and potential questions for interview
First interview	40–110 minutes	Audio recording Notes about thoughts, non-verbal communication and atmosphere after the interview	1–3 hours after the second observation In a nearby office or in the participant's hotel room	Three weeks post-transplantation	Interview guide and questions generated in the first and second observations
Second interview	75–150 minutes.	Audio recording Notes about thoughts, non-verbal communication and atmosphere after the interview	In the participant's home or at a place of their choice	Six months post-transplantation	Life-form interview with focus on everyday experiences Interview guide generated by concepts emerging from the first interview

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involved a close reading of each interview and creating codes that stayed close to the interview data. After this initial phase, a more selective phase began, in which the most significant or frequently occurring codes became focused codes. The focused codes could be short, such as "hierarchy of information resources," or they could be more elaborating codes (Table 3). The coding phase involved interactive work with constant questioning, commenting, and critical reflections around the analysis by writing memos [22]. Through the coding process and memo-writing, the theoretical categories appeared. The focused codes and theoretical categories from the first interview, such as triggers and the hierarchy of resources, were pursued in the second interview through theoretical sampling [22]. Theoretical sampling was used to elaborate and refine theoretical categories, with the goal of saturating the theoretical categories that appear in the trigger-information-response-model [22]. The theoretical codes and the model were developed through constant comparison within and between codes, categories, memos, and the model. All authors agreed on the analysis and the construction of the trigger-information-response model of health literacy.

Ethical considerations

The research project was approved by the Norwegian Regional Committee for Medical and Health Research Ethics (Reference: 2016/1485/REK Sør-Øst C), and by the Data Protection Officer at Oslo University Hospital (Reference: 2016/14592). The Head of the Department of Transplantation Medicine also granted approval.

All participants signed a written informed consent form before participating in the study. The five nurses and six doctors that were observed along with the participants during consultations also signed written informed consent forms.

KGD is a nurse in the transplantation ward but did not have contact with the participants while they were on the ward. Line-by-line coding was employed to avoid having the researcher's assumptions influence the process of analyzing the material [22].

Results

The main categories that appeared during the interviews are presented as an empirical model (Fig 1) that consists of three phases: **the trigger phase**, **the information phase,** and **the**

Table 3. Examples of analysis.

Excerpt from the interview reflecting the theoretical category	Initial coding	Focused coding
Theoretical category: Person in context		
"When you go to the doctor as often as I do now, you can wait with the questions for a day. But if you're going to the doctor in a week or two, you want to find out everything. It's okay to try to find an answer on the internet, but the doctor is best" (9–1)	Frequency of contact and availability of health care providers influence how she decides about a source of information; less availability increases the chance of using other resources that are lower down in the hierarchy—using the internet instead of the doctor	Context and availability are decisive when seeking information
Theoretical category: Trigger–phase		
"When you read all that, everything about those side-effects, you feel sick just by reading about it. But if a side-effect should occur, then maybe. . ." (6–1)	He does not seek information that may cause anxiety without it being necessary	The need of a trigger to seek information
"Every time I meet health care personnel, I forget to ask about it [a wound on her breast], because it doesn't hurt—I can't feel it" (8–2).	The absence of pain makes her forget to seek information about the wound on her breast	Absence of pain—the wound does not trigger enough
Theoretical category: Information–phase		
"Someone told us that you can lose the kidney by getting that biopsy . . . But I knew right away that I would ask the doctor, 'What are the disadvantages or benefits?' It's okay to listen to what others say, but I don't believe everything, so I checked my information with the doctor" (9–1)	Information from fellow patients triggers the need to confirm the information using a resource higher up in the hierarchy	Hierarchy of information resources
"I know them [nurses] very well and call them if I have any questions. So that's where I find or get the information I need. It's mostly the nurses I've had contact with. When I call them they recognize my voice, 'Hey, how are things?" (2–1)	He knows the nurses and they know him—this becomes a natural source of information	Continuity involved mutual knowledge—a natural source of information
Theoretical category: Response–phase		
"You're not as obsessed about it as you were in the beginning perhaps, looking for symptoms or thinking, have I peed less than normal for the last three hours, is there anything wrong now?" (3–2)	He does not look for symptoms—are less sensitive towards situations that may trigger	Sensitivity towards triggers decreased with time and experience
"I realized that after a transplant it was quite normal to put on some weight. You have the risk of getting osteoporosis if you do not walk a little and cycle or exercise a bit (. . .), and diabetes, yes, so we cut out chocolate and sweets, mostly. But that's the reason, otherwise I would probably not have lost weight" (10–2)	The risk of side-effects triggers him to change his diet, start exercising, and lose weight	Information triggered the motivation to change lifestyle

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response phase. The participants were influenced by context and personal factors as they moved between three phases, as information seekers, recipients, and sharers. This study illustrates health literacy as an active process. There is no linear relationship between the three phases, meaning that the response phase could be an endpoint, or a trigger could result in the participant going back and forth between the information phase and the response phase several times.

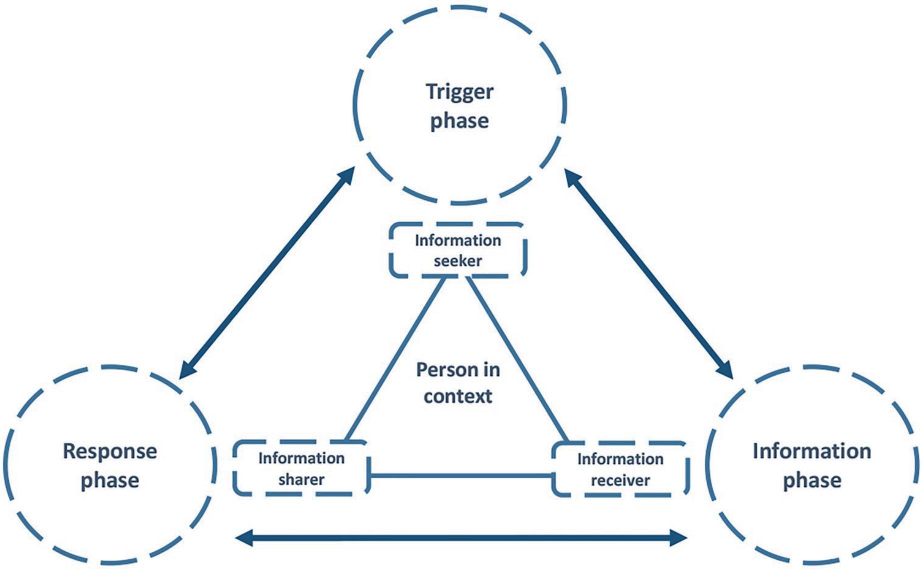

Fig 1. The trigger-information-response model.

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The person in context: Seeking, receiving and sharing information

The person in context constitutes the core of the model and is conceptualized as an information seeker, recipient, and sharer concerning health literacy. However, the person in context comprises contextual factors like social support, place, and time since the transplantation. During their stay at the hospital, health issues were often discussed with fellow patients, and the threshold to approach health professionals was low since the participants had planned consultations several times a week. As the participants traveled back home, health issues and decisions about when and with whom to consult were often discussed with a spouse or other family members. Also, a greater distance to health care professionals naturally increased the threshold for making contact. Context also involved personal factors like experience, knowledge, culture, health condition, expectations, and feelings of responsibility and self-confidence.

As *information seekers*, the participants emphasized the importance of balancing information. The following quote exemplifies the experience of several of the participants, as this participant states what information he needs, but also how he limits the amount of information so as not to become overwhelmed.

> ”I would like to know the creatinine, maybe the urea, but I don’t want a print-out of the blood test results. I prefer to be well when I am well and do other things than go into the disease with things that might trigger anxiety and worries.”
>
> (4-1)

How the participants acted as *information recipients* was influenced by how they preferred to learn, their memory capacity, and the timing of the information. One participant explained how she needed to focus on one thing at a time. It was difficult for her to process information that was more relevant for the future.

> “I didn’t read about transplantation beforehand either. I thought everything has its own time. It was the same when I had to learn about PD [peritoneal dialysis]. I saw it, but I

> couldn't have done it myself. I distanced myself from it. I need to be there. I need to experience it myself. It was too much to take everything in before I was there."
>
> (5-1)

The participants were not passive recipients of information, but also *information sharers*. They expressed having considerable knowledge of and experiences with their health conditions and wanted to be heard.

The trigger phase: The occurrence and interpretation of a health literacy trigger

When exploring what health literacy meant to the participants, triggers appeared as an important concept. A trigger could be an incident or condition that triggered the need to seek and receive information or help, or to share information. As information seekers, the participants considered it important to focus on their normal life, and not on life as a transplant recipient or a patient. Thus, a trigger was an important initiator in the search for information. One participant describes a typical example:

> "Over the past five years, I've been fine with my kidneys. Suddenly everything changed very quickly, then I started searching for more information."
>
> (9-1)

Triggers could also occur when receiving information. For example, during patient education, participants learned that fever could be a sign of organ rejection or infection. This information established a new trigger, which subsequently led the participants to always consult the local nephrologist. Information from other patients could also serve as triggers, such as hearing that a fellow patient's blood test results were better than theirs, thereby creating the need for more information about how to interpret their own results. Symptoms such as pain or fever appeared to be particularly important, both as an information resource and the participants' experiences of triggers. Obtaining information about a health condition without simultaneous bodily symptoms could make the participants interpret the information as less serious and subsequently less triggering. The following quote exemplifies this:

> "My creatinine is a bit high. They [the doctors] think so. I think it is a little odd that I don't feel it. When you don't feel anything, that nothing hurts or anything, I think everything is probably okay."
>
> (1-2)

Triggers were also important when sharing information. One participant had experienced major bleeding as a complication from biopsy and surgery. Her fear of experiencing bleeding again triggered her to always share this information in relevant situations. During the first six months following the transplantation, the participants described a change in their experience of triggers. They described how sensitive they were in the early postoperative phase, where small things became serious triggers. Six months later, with more experience and knowledge, they were less sensitive.

The information phase: Processing information and creating a hierarchy of resources

The information phase explains how the participants made decisions about internal or external resources that could provide information or help when they experienced a health literacy trigger. How the participants chose a resource for information depended on the context, personal factors and how they interpreted the trigger. A resource was *internal* if a participant's personal knowledge and experience were sufficient to respond to a trigger. How the participants chose between *external* resources depended on the experiences of contact and trustworthiness. *Contact* was influenced by language, availability, and threshold. *Trustworthiness* was influenced by the participants' perception of the resource's competence, the feeling of being taken seriously, and their experience of personal connection and usefulness. Finally, *continuity* in health care influenced both contact and trustworthiness.

The nephrologist was a natural information resource for several of the participants. Other typical resources included the general practitioner and other medical specialists, the nurses at the local hospital, written information from the transplant ward, family members, fellow patients and the internet (mostly Google and Facebook). Different triggers generated different needs and gave rise to changes in the resource hierarchy. Making a hierarchy of information resources was a way for participants to select and arrange information, as this participant explains:

> "There is a ton of information. I don't mind that, but it needs to be sorted a little. If you take in and emphasize equally all the information you get from everywhere I think you'll be walking in circles. And therefore, I talk to the doctor, I think he knows best."
>
> (10-1)

To establish a resource, contact had to occur. Speaking the same language was crucial, whether it was the same national language or the doctor translating medical language into one the patient could understand. Availability was a key factor and was experienced very differently from one participant to another. One participants had his nephrologist's private mobile phone number and had a very low threshold for contacting his doctor. Another participant stated that she preferred to consult her general practitioner because the nephrologist was hard to reach:

> "I could call him if there was anything but I don't call a doctor that I have scarcely met before, I cannot [make myself] do that. I started going to my general practitioner."
>
> (7-1)

All the participants talked about having a certain threshold for seeking information or help, especially when consulting the doctor—the trigger had to be perceived as strong enough to warrant crossing that threshold. For some, the threshold could be quite high and the feeling of "bothering" healthcare personnel could be uncomfortable due to low self-confidence. If both availability and self-confidence were low, the trigger needed to be very strong for the participant to make contact. As one participant said,

> "I think I feel like I don't want to bother anyone. There are many things I have never asked about. But I know I have poor self-esteem and that it affects me in many areas."
>
> (8-2)

Trustworthiness depended on the participants' perception of a resource's competence and their feeling of personal connection. The feeling that healthcare personnel did what they could—showing commitment to them as patients and taking them seriously—was essential. The resource also had to be perceived as useful to be at the top of the resource hierarchy. Continuity in care was another factor that repeatedly came up in the interviews and seemed crucial when participants were establishing, choosing, and trusting a resource. This was especially true when choosing to consult healthcare personnel, as continuity ensured the security of being known and sharing common knowledge about the participant's health condition (Table 3).

The response phase: Processing a response

The response phase describes the responses that occurred after the trigger phase and/or after the information phase and depended on how the trigger was perceived by the participant and what kind of information the participant had been seeking, sharing, and giving. The responses the participants described depended on whether the information was interpreted as adequate or not and could result in a search for more information or help from other resources. Questions such as "How long will my kidney last?" were hard to answer and could result in anxiety. One participant experienced discontinuity and a lack of trusted resources in his post-transplant follow-up. This absence of a hierarchy offering alternative resources made him feel paralyzed.

A typical response was a health-related action. One example is a participant who learned about the adverse effect of immunosuppressive medication during patient education and lost 14 kg during the following six months. Information about the risk of cardiovascular disease and obesity became a trigger that was reinforced by observing fellow patients gaining weight during their eight weeks at the patient hotel.

Readjusting sensitivity towards a trigger was another response, as exemplified by one participant who had experienced recurrent episodes of chest pain. This trigger made him seek help at the hospital several times and each time he received the same answer—that nothing was wrong. Experiencing the same trigger several times and repeatedly searching for information slowly changed his response. His sensitivity concerning the information his body gave him decreased because nothing happened, and he developed an explanation as to why the pain occurred and acquired an acceptance of it.

> "I think it's because of all the surgery I had as a kid, I have scars and stuff here [pointing at scars on his chest]. Now I can ignore it completely if I feel any stinging. I've had it for such a long time now without anything bad happening."
>
> (3-2)

An important part of the response was the growing knowledge and experience that became especially evident during the second round of interviews. The knowledge and experience were situated and meaningful for the individual participants and involved a selective process and an interpretation of information based on context and personal factors. One example is a participant who had a prior history of substance abuse. She found that the taking of blood samples from her arm triggered her desire for drugs. She shared this information with a trusted healthcare provider, and together they found a solution that worked, taking blood samples from her foot instead. This knowledge was unique and very important for that participant in her context:

> "Blood samples were taken from my arm and it triggered the whole thing, I just dived into it. This happened every single time, it became so demanding and tiring. But suddenly one day I thought, 'Oh my God, I have feet.' Then I tried my feet. Nothing. I did not notice anything afterward. Now I use my feet every time."
>
> (8-2)

Six months of experience and gathering information had developed the participants' individual knowledge and experience of being kidney transplant recipients, and they knew more about what symptoms were side effects of medications, and what could be signs of organ rejection. Their evolving knowledge made them less sensitive to situations that would have created triggers in the early phase. They also felt more secure about when and where to find information and help.

Discussion

In this Norwegian study, we aimed to elucidate what health literacy may comprise in the context of kidney transplantation, using a qualitative design. The main findings are presented as a model that may offer a supplement to our understanding of health literacy as a process moving between and across a trigger phase, an information phase, and a response phase. During this process, context and personal factors influenced all the three phases: what constituted triggers, how a hierarchy of resources changed and was utilized, and how the participants in the study responded and made decisions about their health. The model also emphasizes the person in context as an information seeker, receiver and sharer.

We found that triggers worked as important facilitators for the participants to start the process of seeking information or help. Jordan et al. [26] also suggest that a "trigger" or a "health event" is needed for people to be motivated to seek out or be receptive to health information. Research on information-seeking behavior has found that individuals must recognize a gap in their knowledge—often signaled by a feeling of anxiety or a need to act—before they are motivated to search for information [27]. Furthermore, Jordan et al. [26] found that prior health experiences and knowledge affect when and where individuals seek information. This supports our findings that experience and knowledge influenced the participants' experience of triggers, and where they went to find information or help. We also found context and other personal factors such as culture, expectations, health condition, feelings of responsibility, and self-confidence to be important inhibitors or facilitators in all three phases of health literacy. For instance, low self-confidence and the desire to avoid being a burden for healthcare providers could prevent some of the participants from addressing their needs, or lead them to seek other sources of information than healthcare professionals. Leung et al. [28] found the same in patients with diabetes; the concern that they might be wasting professionals' time made patients hesitate to indicate their need for health information. If the threshold for making contact is high, it will not only hinder patients from obtaining good-quality information or help, it may also prevent them from acquiring knowledge and create a barrier for good communication with healthcare providers. This may further reduce the opportunity to take an active part in treatment decisions.

In the creation of a resource hierarchy, we found contact, trustworthiness, and continuity of care to be decisive factors that could explain why the participants chose one resource above another. However, we could not rank these factors in order of importance, apart from ascertaining that different triggers required different resources and that this would probably also influence which of the three were most important for the participant. Earlier studies have found that individuals do not necessarily consult the resource that they trust the most, but rather turn to the available ones. For example, people choose the internet due to availability, even when they trust their doctor more [29, 30]. In our study, fever seemed to be the ultimate trigger, always resulting in the participants calling the local nephrologist. Participants were taught repeatedly during patient education that fever should be interpreted as a serious trigger, and our findings emphasize how information may create triggers and motivate patients to establish a resource for help or information.

As information seekers, receivers and sharers, findings indicate that the participants were selective. Selection occurred when participants chose one information resource over another, creating a hierarchy of resources to which they turned in different situations. Selection was also important, as health information was translated into contextual and personal knowledge that was meaningful for the participants. Part of the selection process was also to avoid information that might cause anxiety and stress. The literature on health information-seeking has long been concerned with why people avoid information [31], and both seeking and avoiding information may be motivated by anxiety reduction [32]. An important discussion relates to whether avoiding information may be a sign of having adequate or limited health literacy. In Nutbeam's three categories of health literacy, the most advanced—"critical literacy"—involves critically analyzing information to exert greater control in life events and situations [33]. More information may result in the feeling of losing control, especially if it triggers anxiety. At the same time, this anxiety might be exactly the trigger needed to find more information. The participants were occupied with balancing the information to avoid becoming too involved in potential health issues, and to instead focus on life as "normal", healthy individuals.

Health literacy reflects the ability to gain access to information and help, but this also depends on the health care offered and the possibility of establishing a hierarchy of quality resources. Paasche-Orlow and Wolf [34] argue that the healthcare system might be too complex and difficult for patients to navigate. It may also lack continuity or trustworthy resources, causing people to turn to lesser-quality resources or not search for information at all. The participants in this study emphasized the importance of continuity, contact, and trustworthiness when choosing one resource over another. This is of clinical relevance, as healthcare personnel may focus on how to facilitate continuity, contact, and trustworthiness, and establish a low threshold for making contact. By targeting at these factors, healthcare personnel might reduce existing differences in the utilization of healthcare services, especially when these differences are caused by personal factors such as low levels of self-confidence or a lack of knowledge.

By moving back and forth between the three phases, existing personal experience and knowledge were confronted with new experience and knowledge. In this way, the participants evolved an individual knowledge and experience that was meaningful in specific contexts. Lonergan [35] uses the verb «knowing» instead of the noun "knowledge", and suggests that knowledge is not something you discover but an activity—"something that you *do"* (p.529). This may be transferred to the contextual knowledge and experience that the participants developed through the active process of moving between the phases. Knowledge is found to be an essential part of health literacy but is usually described more generally as a set of skills [36], such as having a certain vocabulary for and conceptual knowledge about how the body works [37]. This kind of knowledge is more visible and easier to measure and influence with interventions. The more situated "knowing" is nevertheless an important part of health literacy, and exploring this knowing might give us a better understanding of the complexity and factors that influence health literacy.

Our empirical model focuses on when, why, and how the kidney transplant recipient decide to seek, receive or share information. These results contribute important knowledge to clinical practice. A deeper understanding of triggers as important initiators in health literacy, and the mechanisms behind choosing a resource for help or information, might be transferable to other kidney transplant recipients and give us a broader understanding of what *motivates* in the process of searching for, receiving, and sharing information.

Strengths and weaknesses of the study

Few studies explore health literacy qualitatively through patient experiences, and currently, this study seems to be one of the few to explore health literacy in the context of kidney transplant recipients. As such, this study helps fill an important knowledge gap. There is an increasing number of kidney transplant recipients of non-Norwegian ethnicity, and existing research indicates that ethnic subgroups might experience several challenges related to finding, understanding, and using health information. Language and cultural barriers may also hinder good communication with healthcare providers. This study only includes one participant of non-Norwegian ethnicity and does not provide comprehensive knowledge about how this affects health literacy in the context of kidney transplant recipients. Hence, additional studies are needed to explore health literacy in different ethnic subgroups.

Supporting information

S1 Table. Participants answers to the Health Literacy Questionnaire.
(DOCX)

S2 Table. Interview guide 1 and 2.
(DOCX)

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