



Health-Related Quality of Life and Patient Reported Outcome Measures Following Transplantation Surgery

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Introduction

Transplantation surgery represents one of the greatest achievements in modern medicine. Solid organ transplantation in patients with end-stage organ failure promises not only to extend life but to improve its quality. Nevertheless, the presence of new challenges, such as ageing populations with multiple comorbidities and the organ shortage crisis have the potential to significantly influence outcomes in transplantation [1]. Furthermore, each patient journey follows a unique course, influenced by a plethora of biological, psychological, and social variables. These have the capacity to influence patients' perception of the value of transplantation. Health-Related Quality of Life (HRQOL) outcomes and Patient-Reported Outcome Measures (PROMs) aim to be tools to capture the unique features of each case and confer insights into the ways in which transplantation can affect different groups, allowing us to address new challenges with greater preparedness.

This chapter presents the effects of solid organ transplantation (kidney, liver, heart, lung) on the

quality of life of recipients and living donors. Studies reporting on pancreas transplantation are included in the section discussing kidney transplantation, as most studies report on outcomes for simultaneous kidney-pancreas recipients. A similar approach has been used with regard to small bowel transplantation, which are most commonly performed in the context of combined liver-bowel transplants.

Background

The Role of HRQOL-PROMS in Transplantation

Elective and emergency operations constitute one of the largest and most resource-demanding elements in healthcare. Therefore, it is essential to optimise the efficiency and effectiveness of the associated clinical pathways. QoL outcomes and PROMs can be used to inform quality improvement initiatives and improve decision making regarding the allocation of resources and the direction of efforts.

In 2009, the Department of Health in the United Kingdom mandated the inclusion of PROMs as service delivery metrics for certain elective surgical procedures [2]. On a global scale, the International Consortium for Health Outcomes Measurement (ICHOM) has reiterated the importance of incorporating PROMS as

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tools to measure HRQOL in promoting ‘value-based’ outcome measures and developing international standards of quality assurance in transplantation [3].

In the context of transplantation, monitoring patient progress through clinical criteria or biomarker reports provides myopic insights into the impact of a disease or treatment on the patient and their quality of life. Formal outcome measures aim to capture the perceived success of transplantation from the patients’ perspective. For instance, patients may report low HRQOL despite a well-functioning graft [4]. In addition, in recent decades, there has been an overall practical and ideological shift in the role of transplantation from longevity-oriented outcomes to a tool for transforming HRQOL. Pivotal to this paradigm shift are the organ shortage crisis and the evolving patient demographics, with a rise of older transplant recipients and the increased use of grafts from ‘sub-optimal’ or extended criteria donors [5]. Consequently, HRQOL-PROMS data provide patients with the opportunity to report their symptom-burden and treatment-burden effects. Such insights are invaluable for health-

care systems aiming to foster a patient-centred approach and allowing transplant programmes to evolve and adapt to the needs and demands of patients [6]. Notably, HRQOL and PROMS are different to approaches such as Patient Reported Experience Measures (PREMS) that aim to capture the views of the patients regarding specific elements of service provision (i.e. quality of the hospital facilities, friendliness of the staff) and do not capture patient experience related to a specific therapeutic intervention.

Assessment Tools for Measuring HRQOL-PROMS in Transplantation

HRQOL-PROMS tools aim to provide an ‘aerial’ view of a patient’s physical, mental and social wellbeing as well as life-participation, through formal assessment tools with validated psychometric properties. Such tools can be subdivided into generic (e.g. SF-36, EQ-5D, PROMIS-29 etc.) [7–9] and disease-specific or symptom specific instruments (e.g. BDI, ESRD-SCL etc.) [10, 11] (Fig. 14.1).

Holistic QoL Assessments

- SF-36 (Vitality, physical functioning, bodily pain, general health, physical role functioning, emotional role functioning, social role functioning and mental health)
- SF-12 is a condensed version covering similar domains
- EQ-5D (Mobility, self-care, usual activities, pain/discomfort, anxiety/depression and global health)
- PROMIS-29 (Depression, anxiety, physical function, pain interference, fatigue, sleep disturbance and ability to participate in social roles and activities)
- WHOQOL-100 (Physical, psychological, level of independence, social relationships, environment, spirituality.) etc.

Disease Specific Assessments

- e.g. KTQ, Minnesota Living with Heart Failure Questionnaire, Liver Disease QOL etc.
- Can be used in independently or as adjuncts to generic HRQOL PROMS tools.

Symptom Specific Assessments

- Can report single symptoms e.g. Hospital Anxiety and Depression Score (HADS), Beck Depression Inventory (BDI) etc., Fatigue Severity Scale.

Fig. 14.1 General HRQOL PROMS, disease-specific PROMS and symptom-specific PROMS tools

The choice of instrument depends on logistical factors, such as:

- Time available for completion
- Response burden (the amount of effort or input required from the patient to complete the questionnaire)
- Infrastructure available to implement and interpret questionnaires
- Ability to sustain consistent follow up
- Patient factors (e.g. literacy levels, cognitive function, access to electronic devices etc.)
- Research domains that healthcare professionals wish to investigate.

Studies may also choose to combine a generic QoL tool and a disease or symptom specific tool to provide both a specific and holistic view of the issue being examined. To achieve the greatest impact, HRQOL should be measured at regular intervals, allowing for identification of trends and clinically meaningful changes in health and/or disease status over time, also known as the ‘responsiveness’ of the instrument [12, 13].

Materials and Methods

Search Strategy

A systematic search was conducted in August-September 2021 using PubMed, using the following search terms: (‘patient-reported outcome measures’ OR ‘patient-reported outcome’) OR (‘quality of life’ OR ‘Health-Related Quality of Life’ OR ‘QoL’ OR ‘HRQOL’) AND (‘transplantation’ OR ‘kidney transplant’ OR ‘liver transplant’ OR ‘lung transplant’ OR ‘heart transplant’). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed [14, 15].

Inclusion/Exclusion Criteria

There were no limitations set on the type of transplantation, sample size or date of study completion. Articles relating to solid organ

transplantation were included. Case reports and review articles were excluded. Articles about ‘autologous transplantation’ and allotransplantation were included. Articles that were not in English were excluded.

Outcomes of Interest and Data Extraction

From each study, the following data was extracted: author, year of publication, data collection period, study type, study objectives, sample size, location of study, type of transplant, participant characteristics, evidence of pre-operative HRQOL assessment and follow-up HRQOL, intervals at which HRQOL was measured, HRQOL instrument, completion, non-HRQOL outcomes, main HRQOL findings and study quality (Table 14.1).

Quality Score

The methodological quality of studies was assessed using a standardised 10-item checklist, as reported by Tan et al. [15].

Table 14.1 Methodological quality scoring criteria (adapted from [15])

| | |
|---|--|
| A | Socio-demographic and medical data are described (e.g. age, race etc.) |
| B | Inclusion and/or exclusion criteria formulated |
| C | The process of data collection is described (e.g. interview or self-report) |
| D | The results are compared between two groups or more (e.g. healthy populations, groups with different treatments or ages) |
| E | Participation and response rates for groups have to be described as >75% |
| F | Information is presented about patient/disease characteristics of respondents and non-respondents |
| G | A standardised or valid QOL questionnaire is used |
| H | Results are not only described for QOL but also the physical, psychological and social domains |
| I | Mean, median, standard deviations or percentages are reported for most of the outcome measures |
| J | Patients signed an informed consent form before study participation |

Results

The initial literature search produced 541 results. Based on the inclusion/exclusion criteria, 178 papers were included in the final analysis (kidney transplantation = 33.7%, liver transplantation = 43.8%, Heart transplantation = 10.7%, Lung transplantation = 11.8%). The total number of patients from all the papers was 44420.

The vast majority of papers were prospective and observational studies (67.6%). From all the papers, a cross-sectional design (64.6%) or a cohort design (32%). A small proportion were randomised controlled trials (2.8%). Quality scores ranged from 2 to 9, with an average score of 7. A pre-operative assessment was only performed in 24% of studies.

Most studies used more than one instrument, often combining general and symptom-specific questionnaires. A summary of the different HRQOL instruments encountered in different studies included in this review can be found in Table 14.2, and Figs. 14.2 and 14.3.

HRQOL and PROMS in Kidney Transplantation

Background

Renal transplantation is a catalytic therapeutic intervention in patients with end-stage renal disease (ESRD). Before accessing transplantation, patients are started on renal replacement therapy (RRT) and are placed on the waiting list until an organ is available. The matching process takes into consideration patient characteristics, such as age and comorbidities. However, the non-standardised candidate evaluation criteria are frequently centre-specific, resulting in disparities in waiting periods and variable time on RRT. This means that there is significant variation in the health status and characteristics of transplant candidates. In recent decades, there have been efforts to lower transplantation thresholds and offer grafts to older or medically complex patients. This potentially influences patient and graft survival, as well as the incidence of hospital readmissions and quality of life outcomes [16].

Table 14.2 Disease specific and symptom specific HRQOL-PROM instruments

| Organ | Disease specific HRQOL-PROM instruments | Symptom-specific |
|--------|---|------------------|
| Kidney | ReTransQoL KDQOL-SF KTQ-25 TxEQ | 30/60 |
| Liver | EUROTOLD PeLTQL SF-LDQ LDQOL-Q NIDDK-QOL CLDQ | 36/78 |
| Heart | Heart Transplant stressor scale Organ Transplant Symptom and Wellbeing Instrument Cardiac specific Ferrans and Powers' Quality of Life Minnesota Living with Heart Failure questionnaire | Nov-19 |
| Lung | TxEQ-D SGRQ Borg Symptoms Score | 17/21 |

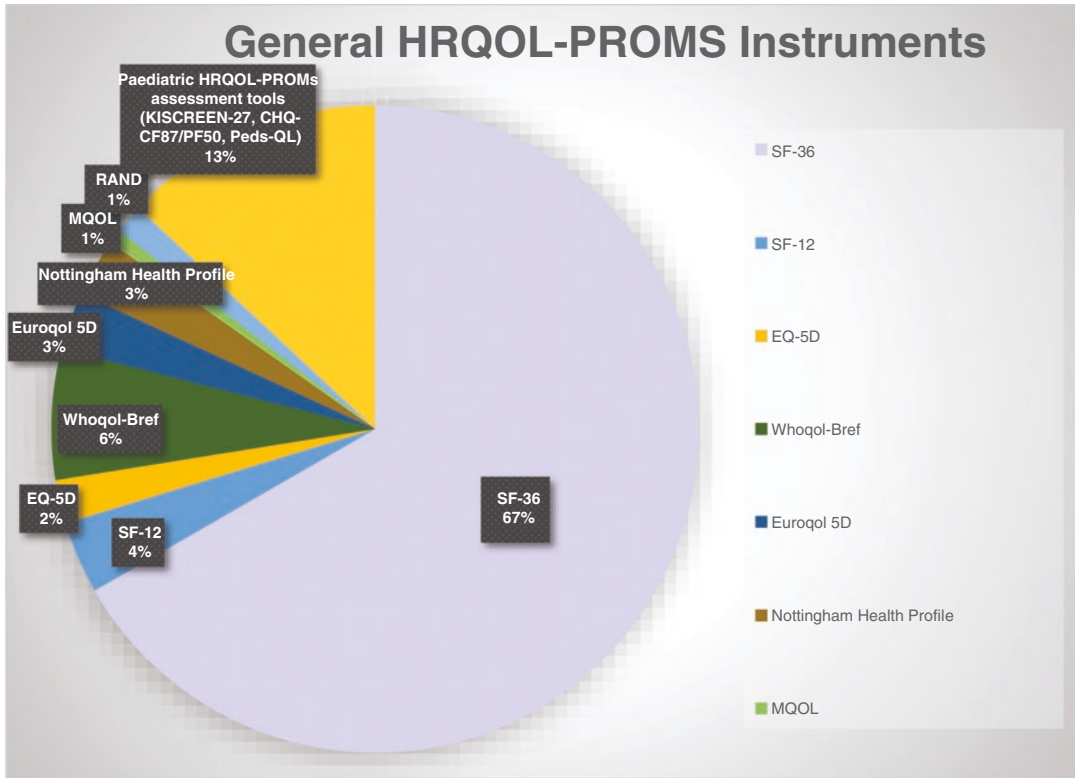


Fig. 14.2 Summary of the general HRQOL PROMS tools included

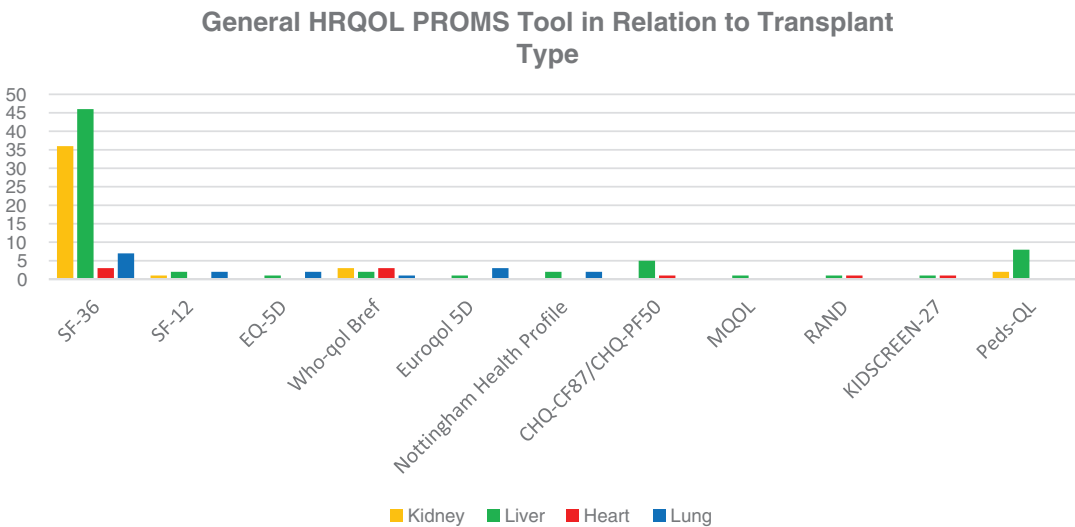


Fig. 14.3 General HRQOL PROMS instruments used-solid organ breakdown



Fig. 14.4 Summary of HRQOL-PROMs in kidney transplantation

Overall QoL Outcomes

A summary of the factors affecting HRQOL in kidney transplant patients can be found in Fig. 14.4. Overall, kidney transplantation improves the physical health and fitness outcomes. There is mixed evidence about the QoL outcomes of renal transplant recipients compared to those of the general population and compared to other solid organ transplant recipients [17–19]. This may be due an emphasis on clinical post-operative outcomes and end-points such as cessation of dialysis, as well as biomarker criteria e.g. reduction in creatinine, rather than QoL outcomes

and post-operative support [18, 19]. Furthermore, adverse transplant outcomes, such as graft failure, leading to re-commencement of dialysis or RRT does not lead to a significant reduction in QoL compared to the pre-transplant status, as these patients scored similarly to patients not previously transplanted [18, 19]. Post-transplant factors that influence QoL include medication non-adherence and the presence of medical complications or critical illness [20]. In addition, problematic psychological processing of the life-changing transplant event is a risk factor for non-adherence to post-transplant regimens [21].

Disease-Related Symptom Burden

Disease-specific symptoms relating to ESRD, including uraemia associated symptoms, neuromuscular and dermatological complaints and bodily pain improve after renal transplantation [22, 23]. Fatigue is one of the most common complaints amongst ESRD patients. Neto et al. [24] reported that greater fatigue symptom severity is influenced by certain pre-transplantation patient characteristics, such as high BMI, ESRD secondary to glomerulonephritis, as well as post-transplant factors, such as combined organ transplantation.

Post-transplant anxiety has the potential to give rise to new symptoms [25]. For instance, high-levels of anxiety and depression after renal transplantation give rise to additional comorbidities, such as psychogenic erectile dysfunction (ED) in male recipients [26]. The impact of post-transplant anxiety is also evidence in the high incidence of sleep-related disturbances [27, 28]. Brekke et al. [29], Silva et al. [30] and Russcher et al. [31] report that whilst sleep disturbances such as daytime sleepiness are highly reported amongst ESRD and haemodialysis patients, these improve after transplantation, nevertheless, sleep quality remains poor in renal transplant recipients compared to the general population.

The significant adverse impact of anxiety in all domains of recipient QoL, suggest a need for better screening and management of psychiatric symptoms [32]. However, the most significant determinant of recipient mental health may be personal cognitive and psychological processing strategies regarding the transplant event [33].

Female kidney transplant recipients also face unique challenges such as infertility and obstetric complications [34]. Whilst successful pregnancy resulting in live-birth was attainable (with a mean interval between transplantation and pregnancy was 41 months), there was also a high incidence of complications during pregnancy, such as anaemia and pre-eclampsia. The incidence of graft loss and impaired graft function 2 years after pregnancy occurred in a small-subset of patients. Female recipients are also more likely to report low energy and fatigue and lower overall quality of life [35, 36].

Immunosuppressive therapy related side-effects and costs can be amongst the most significant contributors to adverse outcomes for post-transplant quality of life, especially in female patients [33, 37]. Madariaga et al. [38] compared the effects of achieving tolerance by bone marrow treatment to conventional immunosuppressive regimens and concluded that patients who achieved tolerance had a significantly lower incidence of complications and comorbidities. These patients also had higher disease specific HRQOL scores.

Patients with type 1 diabetes mellitus who receive a simultaneous kidney-pancreas transplant (SPKT) experience better QoL than patients on the waiting list [39]. However, QoL outcomes for SKPT are lowest among female recipients [40]. There is some evidence to suggest that peritoneal dialysis prior to SPKT results in better QoL outcomes compared to patients who undergo haemodialysis [41].

Physical Health Outcomes

However, several factors predict negative or adverse outcomes regarding physical health, such as low levels of pre-operative fitness, frailty, and post-operative steroid use [42]. Nevertheless, McAdams DeMarco et al. [43] demonstrated that patients who were already frail pre-transplant experienced a significant improvement in physical functionality and physiological reserve post-transplant. The self-assessed disease specific HRQOL of these patients was also higher compared to non-frail patients, suggesting that transplantation results in considerable improvement from baseline. Other factors influencing the capacity for physical exercise include post-operative medication regimens. Painter et al. [44] highlighted that post-transplant steroids can limit exercise capacity due to limited muscle strength, resulting in overall lower exercise capacity one-year post-transplant.

Griva et al. [45] proposed that physical fitness scores and level of physical activity are influenced by donor-type, with living-related transplant recipients reporting reduced physical functioning score, compared to cadaveric recipients. Broers et al. [46] suggested that this is not

related to issues with the quality of grafts from living-donors and does not reflect a need for greater screening measures for living donors as this relationship is more likely related to psychological factors, such as feelings of responsibility and worry about damaging the transplant, leading to overly cautious behaviours. This seems to be a wider issue affecting renal transplant recipients as despite having greater capacity to engage in more physical activity, many kidney transplant recipients choose not to modify their activity levels. For instance, Gordon et al. [47] reported that up to 76% of patients in their study were sedentary and only 11% were exercising regularly or at the recommended level for their age group and baseline.

Mental Health After Kidney Transplantation

Despite the aforementioned evidence regarding the complications of post-transplant anxiety, Dweib et al. [48] reported that uncertainty about the future and fear of graft failure were not significant factors contributing to lower mental components scores on HRQOL questionnaires. Furthermore, Andrade et al. [49] reported that there was no difference in the presence of significant psychiatric co-morbidities such as moderate-severe depression and suicidal ideation in renal transplant patients and patients who were stable on haemodialysis treatment.

Mouelhi et al. [50] reported that several psycho-social variables predicted the incidence of mental health problems post-renal transplant, including lack of social support and being on antidepressants. This suggests that non-pharmacological interventions, such as psychotherapy, to improve recipient mental health need to be explored. A randomised-controlled study by Baines et al. [51] revealed that there is significant therapeutic benefit in both individual and group psychotherapy in improving mental health scores in renal transplant recipients.

Employability and Social-Wellbeing Outcomes

With regard to overall HRQOL, Alhussain et al. [52] reported that male transplant recipients are

more likely to achieve employability and higher work satisfaction scores. Socio-economic background and level of education have a significant influence on post-operative quality of life, as patients from low-income households experience prolonged recovery periods and a higher incidence of anxiety and depression ([53, 54]).

Grubman-Nowak et al. [55] report that employment is associated with improved overall life quality. Specifically, Schmid et al. [56] suggested that return to employment and disease-specific quality of life were only improved in patients who achieved good levels of adherence to treatment. Nevertheless, post-transplant employability is also significantly influenced by a recipient's mindset and personality. For instance, patients who perceive themselves as more independent and self-reliant are more likely to be in full-time employment. As such, evaluation of recipient psychosocial characteristics and self-perceived independence can be valuable for predicting engagement with occupational activation programs and identifying groups of patients who may require more psychosocial support [57].

Donor Quality of Life Post-Donation

Overall, HRQOL in living donors is far superior to that of the general population, possibly due to the fact that donors are overall healthy and active individuals and also due to all the post-donation support services [58]. However, there is evidence to suggest that donation leads to a temporary reduction in the HRQOL of donors in the first six weeks after donation [59]. This may be related to the fact that donors often felt that the pain intensity was worse than expected and recovery times were slower than anticipated [60]. Subsequently, whilst donors are at least as satisfied with their lives as the general population, achieving comparable scores across multiple quality of life domains, many donors also experience a reduction from their personal baseline [61]. Other factors influencing donor QoL outcomes include the type of donor nephrectomy technique used which is also a significant factor related to donor wellbeing, with laparoscopic nephrectomy resulting

in superior donor quality of life compared to open nephrectomy [62].

Overall, living kidney donors had no regrets about the procedure, regardless of whether they were donating to a relative or altruistically and in living-related cases, the process enhanced donor-recipient relationships [63]. The main factor contributing to feelings of regret were graft failure or adverse outcomes for the recipient [64, 65], however, overall, this does not have a significant adverse impact on donor quality of life or HRQOL scores [66]. More significant is the effect of donor perioperative or post-operative complications, which can lead to a temporary reduction in quality of life due to psychological, rather than physical health concerns in the first 3 months post-donation [67].

Finally, Sommerer et al. [58] and Ay et al. [68] reported that non-modifiable donor characteristics, such as gender may predispose to lower self-perceived HRQOL, with middle-aged female donors identified as the most vulnerable group for worse QoL outcomes. In addition, non-White race, obesity and previous psychiatric history were contributing factors towards adverse clinical outcomes and reduced HRQOL in kidney donors, specifically in relation to physical function [69].

Paediatric Transplantation

Overall, there is consensus amongst paediatric patients and caregivers about overall improvement in HRQOL. As reported by Rotella et al. [70], the most significant improvement was seen in physical function and subjective energy levels. Caregivers of paediatric transplant recipients are also more likely to report improvements in social domains, such as school/education [71]. However, there may be a disparity in the parental perception of their child's mental health and the reality, as reported by the patients, as well as a difference in early post-transplant versus long-term quality of life [72]. Van Pilsum Rasmussen [73] et al reported that carer quality of life and care-burden appeared comparable before and after renal transplantation.

There is strong evidence to suggest that paediatric recipients should receive greater long-term psychological support, as many patients experi-

enced a significantly higher incidence of mental health problems, negative self-image perception, related to physical appearance and above average BMI scores at 2- and 16-years post-transplantation compared to healthy controls [74]. Subsequently, post-transplant care should focus on improving physical activity in children to alleviate the incidence of psychological co-morbidities in order to prevent additional problems in physical health.

Adult who had a kidney transplant as children are also more likely to experience stunting of their social development due to poor psychosocial adjustment. Such patients had fewer higher education qualifications and higher rates of unemployment. Former paediatric transplant recipients are also less likely to have personal relationships outside of the family, suggesting a greater need for support in post-transplant psychological processing in paediatric patients [75].

HRQOL & PROMS in Liver Transplantation

Background

Liver transplantation is second to renal transplantation as the most commonly performed transplant. The main indications for liver transplantation are end-stage liver disease (ESLD) (due to either alcohol-related or non-alcohol related disease) and acute liver failure. Similarly to kidney transplantation, liver allografts can be retrieved from both living and deceased donors.

Overall QoL

A summary of the factors influencing HRQOL in liver transplant recipients can be found in Fig. 14.5. Liver transplant recipients experience a marked improvement in overall QoL compared to patients with ESLD [76]. However, long-term survival (>15 years after transplantation) is associated with a significant, progressive reduction in patient quality of life compared to the general population ([77].). There are also certain socio-demographic factors that act as predictors of adverse QoL outcomes, the most significant of which are older age and female gender [78, 79]. There is also evidence to suggest that pre-

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| <p>Overall</p> <ul style="list-style-type: none"> • Liver transplantation improves overall HRQOL, however, the positive effects diminish over time, especially in older and female patients. • Transplant factors that influence outcomes include ESLD secondary to alcoholic liver disease and DCD grafts. However, strict donor screening does not have a significant effect on outcomes. |
| <p>Symptom-Burden</p> <ul style="list-style-type: none"> • ESLD symptoms improve however, high incidence of immunosuppression-related symptom burden e.g. headaches. • Temporary reduction deterioration in cognitive function after transplantation which fully resolves. • Fatigue is the most significant symptom in both ESLD and liver transplant patients. |
| <p>Physical Health</p> <ul style="list-style-type: none"> • Preoperative frailty or poor baseline fitness are predictive of mortality risk and impaired physical health after transplantation. • Gender, rather than age, is the most significant predictor of frailty, with worse outcomes in female recipients. |
| <p>Mental Health</p> <ul style="list-style-type: none"> • Liver transplant recipients have better mental health than ESLD patients from 3-months post-transplant. • However, before this effect is observed, there is an increased risk of anxiety and PTSD. In most cases, this is related to fear of graft loss. • Lack of social support predicts poor QoL as well as adverse medical outcomes, including mortality risk. |
| <p>Employment and Social Outcomes</p> <ul style="list-style-type: none"> • Factors that impair recipients' ability to accomplish social and productive lives include medical issues or high symptom-burden e.g. fatigue, weakness and psychosocial characteristics e.g. female gender, aged >60. |
| <p>Paediatric Outcomes</p> <ul style="list-style-type: none"> • QoL is comparable to children with chronic illness but below that of healthy controls. • Non-Caucasian, teenage and sedentary patients with parents from a lower socio-economic background and lower educational level are at highest risk of impaired QoL, with high-levels of transplant related-disability. |
| <p>Donor Outcomes</p> <ul style="list-style-type: none"> • In the long-term, living donor satisfaction with life, mental and physical health are greater than in the general population. • Donor attitudes, such as the belief in the value of donation and improved self-image positively influence outcomes. Female donors are more likely to suffer from depression after donation. • Temporary increase in physical health complaints immediately after donation, specifically with regard to bodily pain. |

Fig. 14.5 Summary of HRQOL and PROMs in liver transplantation

transplant factors, such as ESLD secondary to alcohol-related liver disease and peri-transplant factors, such as grafts from donors after circulatory death (DCD) adversely impact long-term QoL outcomes [80]. With regard to living donation, there is little value to strict donor-risk stratification measures as this has little effect on recipient overall QoL [81]. Re-transplantation after graft failure has a significant adverse impact on recipient QoL [82].

Disease-Related Symptom Burden

Recipient symptom reporting changes depend on the time after transplantation. Overall, patients reported fewer ESLD-related symptoms and improved ability to manage daily activities [83,

84]. However, patients may experience distress in the presence of new symptoms, such as hyperphagia, trembling and headaches, which may be related to post-operative immunosuppression regimen side-effects [85]. Furthermore, there is a significant risk of temporary deterioration in cognitive function in the early stages after transplantation [86]. This transient deterioration has no long-term sequelae and after 3-months, there is a profound, sustained improvement in recipient cognition in transplant recipients compared to patients on the waiting list [87].

Fatigue remains one of the most significant symptoms among liver transplant recipients. Aadahl et al. [88] suggested that fatigue is most likely due to organic causes, rather than non-

organic or psychological pathology. However, levels of fatigue were lower in liver transplant recipients, compared to pre-transplant or ESLD patients, leading to a net improvement in HRQOL [89]. Finally, similarly to renal transplant recipients, liver transplant recipients are more likely to experience anxiety related sleep disturbances [90–92].

Physical Health

Most studies report on good overall physical fitness after liver transplantation, with levels comparable to those of the general population [93–95]. However, the positive impact of transplantation on physical fitness diminished beyond 5 years [96]. Maintaining cardiorespiratory fitness is possible through structured exercise programmes, which also improve recipient mental health and self-image [97]. There is value in pre-operative assessment of baseline physical fitness as this can identify which groups are at high-risk of mortality and lower physical health scores after transplantation [98].

With regard to socio-demographic characteristics, female patients are more likely to report significantly lower HRQOL scores especially with regard to physical domains, whilst higher educational background is associated with improved HRQOL [99]. There is no evidence to suggest that older recipients experience significantly worse outcomes relating to physical function or disability compared to younger recipients [100].

Mental Health Outcomes

Liver-transplant recipients experience a significant, long-term improvement in symptoms of depression or anxiety after the transplant [95, 101, 102]. This is accompanied by an improved outlook on life and greater sense of optimism [103]. This benefit on recipient mental health is most prominent in patients with less severe chronic liver disease scores or in cases where there was a history of alcoholic liver disease [104].

However, it takes approximately 3-months to achieve this positive impact on recipient mental health [105]. Until this is reached, the first 3 months are considered a ‘high-risk’ period for

psychiatric symptoms. Notably, liver transplant recipients are more likely to suffer from anxiety and post-traumatic stress disorder, possibly relating to fear of graft loss [106–108].

Predictors of adverse mental health outcomes after liver transplantation include recipient personality type (e.g. anxious-avoidant behaviours), poor medication compliance and substance abuse [109, 110]. Lack of social support is one of the most important psychosocial factors which influence both mental health outcomes and overall mortality-risk [104, 111]. In contrast active coping strategies and good social support are associated with reduced length of hospital stay and better physical health outcomes. Finally, patients with baseline, pre-transplant depression or anxiety are more likely to report incomplete recovery in symptoms [112–114].

Employment and Social Outcomes

Female recipients aged 60 years and above have the lowest self-perceived levels of social functioning and satisfaction with QoL compared to age matched male recipients [115–117].

There is no difference in the social reintegration patterns of patients based on original indication for transplantation (e.g. alcoholic liver disease versus non-alcoholic liver disease), with both groups being able to accomplish social and productive lives [99]. However, persistence of symptoms such as chronic fatigue and weakness can hinder employment and social integration [118]. This was supported by Saab et al. [119], who suggested that good baseline levels of pre-operative fitness and the absence of significant co-morbidities significantly improve employment prospects. This can be useful for predicting which patients would require more support for securing employment post-transplant.

Paediatric Transplantation

Overall, the QoL of paediatric liver transplant recipients is significantly lower than that of the general population, but similar to that of children with chronic illnesses [120, 121]. Predictors of poor HRQOL outcomes include worse baseline physical health, lower levels of physical activity, older age at transplantation, lower maternal education levels, recipient not being in full-time educa-

tion and non-Caucasian patients [122–127]. There is also often a mismatch between parental and patient perception of the value of transplantation on quality of life, with parents more likely to judge their children's HRQOL as 'impaired' [128, 129]. Despite this, anxiety and depression rates were significantly lower in paediatric liver transplant recipients than in healthy controls [130–132].

One of the major contributors to low QoL scores is the high incidence of post-transplant sleep related disturbances, as this affects several parameters, such as fatigue, energy and school functioning [133]. Other significant challenges for former paediatric patients are medication compliance, independence, and motivation to commit to self-care routines and concerns about exercise restrictions [134, 135]. Transplantation does not limit recipient growth, regardless of whether patients received split-liver allografts or whole-sized grafts [136].

Paediatric patients that survive into adulthood have lower physical HRQOL compared to the general population and experience significant levels of transplant-related disability [137–140].

Donor Outcomes

Overall, the QoL of living liver donors is significantly higher than the general population, specifically with regard to physical and mental health [141]. In addition, donor satisfaction with the donation process was high, regardless of whether post-operative complications were experienced [142, 143]. This was influenced by the belief that the donation was worthwhile and the perception that one becomes a 'better person' after donation [144].

Factors negatively impacting post-donation quality of life include concerns about returning to work, a perceived inadequacy of preoperative information and self-consciousness about bodily change [103, 145]. In addition, several donors express the feeling that postoperative pain was much higher than that which was anticipated pre-donation [146, 147]. However, this effect is only temporary, as physical complaints are only present for up to 1-month after donation, subsequently returning to baseline level [148]. However, female donors are more likely to experience mental health problems, such as depression, after donation [149, 150].

There was no difference in donor outcomes in right-lobe versus left-lobe donation [151, 152]

Heart and Lung Transplantation

Background

Heart transplantation is indicated for patients with end-stage heart failure (HF), suffering from debilitating symptoms that are refractory to medical therapy. Underlying conditions that may contribute to refractory HF include cardiomyopathy, acquired/ coronary artery disease, congenital heart disease or previous graft failure. HF patients are carefully screened, and risk stratified in order to identify the individuals who are most likely to survive and benefit from the procedure. Pre-transplant evaluation criteria often rely on baseline physical function and exercise testing, often using tools such as the New York Heart Association (NYHA) classification or objective measures of physiological reserve, such as exercise capacity testing by measuring peak VO₂.

Lung transplantation is primarily indicated for respiratory insufficiency as a result of chronic restrictive or chronic obstructive pathology. The type of lung transplant, single versus double is also dependent upon the underlying disease process. For example, patients with cystic fibrosis are inherently eligible for double lung transplantation (DLT), whilst fibrotic or chronic obstructive pathology patients may experience good clinical outcomes with a single lung transplant (SLT). As the volume of lung transplantation has increased in the last decades, performing two SLTs has the potential to benefit two patients.

Symptom-Burden and Physical Functionality After Cardiac Transplantation

Post-transplantation symptom burden after transplantation comprises mainly autonomic disturbances, such as diaphoresis, tremor, and sexual dysfunction. These are both the most common and most distressing symptoms, and these primarily impact older cardiac transplant recipients [153]. Symptom-burden improves 5–10 years after heart transplantation, with symptoms either completely resolving or classified as 'mild', with

no impact on functional capacity [154]. This may be because it takes approximately 2-years to establish sufficient graft parasympathetic innervation [155]. Psychosocial predictors of physical disability and poor physical health include female gender, lower educational status, and unemployment. Physical health issues and comorbidities that influence outcomes include diabetes, obesity, mental health problems and frailty and orthopaedic problems [154, 156].

Cardiac transplant recipients can self-appraise their personal physical health and fitness accurately and most have good capacity for both endurance and high-intensity interval training [157].

Psychosocial Outcomes After Cardiac Transplantation

There is a high incidence of mental health symptoms, such as depression and anxiety, in cardiac transplant recipients and these may be the greatest contributors to low HRQOL, [158]. This may be related to the high rates of preoperative psychopathology [159]. However, most patients only suffer from 'mild' depression and that the most important predictors of poor mental health were inadequate or 'problem-focused' coping strategies or a low sense of 'control' in relation to the transplant events [160].

This is particularly true for female recipients, who also reported greater feelings of 'hopelessness' and difficulty adhering to treatment regimens [154, 161]. Conversely, De Aguiar et al. [162] found that compared to male recipients, female recipients experienced greater satisfaction with social support networks in place after transplantation [163].

Paediatric Cardiac Transplantation

Paediatric patients who undergo heart transplantation for severe biventricular illness are able to obtain subjectively high levels of quality of life across all physical, emotional and social domains [164, 165]. However, in long-term follow-up of paediatric cardiac transplant recipients into adulthood, Sepke et al. [166] reported that recipients are more likely to maintain close, dependent relationships with their parents and chose to live in close proximity to their 'primary caregivers'. Nevertheless, former paediatric heart transplant recipients have better employment status than peers of the same age, being more likely to be in full time employment.

There is a close relationship between paediatric recipient QoL and that of their primary caregiver. For instance, recipients whose caregivers perceived their own general health as 'below average' had poorer survival rates at one year and seven years after transplantation [167, 168]. Both paediatric patients and their parents agreed that there is a need to simplify therapeutic management and promote self-sufficiency, as frequent medication changes and multiple clinic appointments adversely impact HRQOL [169]. In semi-structured interviews with paediatric transplant recipients and their families, Anthony et al. [170] found that there was a nearly unanimous endorsement of electronic PROMS tools and remote reporting, patients and their parents agreed that this would be suitable for patients aged 8–10 years or older. The key findings for this section are summarised in Fig. 14.6.

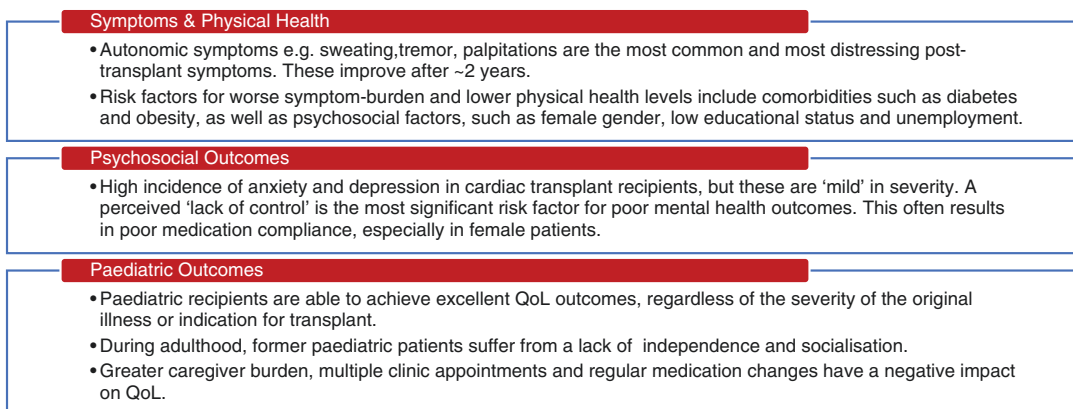


Fig. 14.6 Summary of HRQOL and PROMs in cardiac transplantation

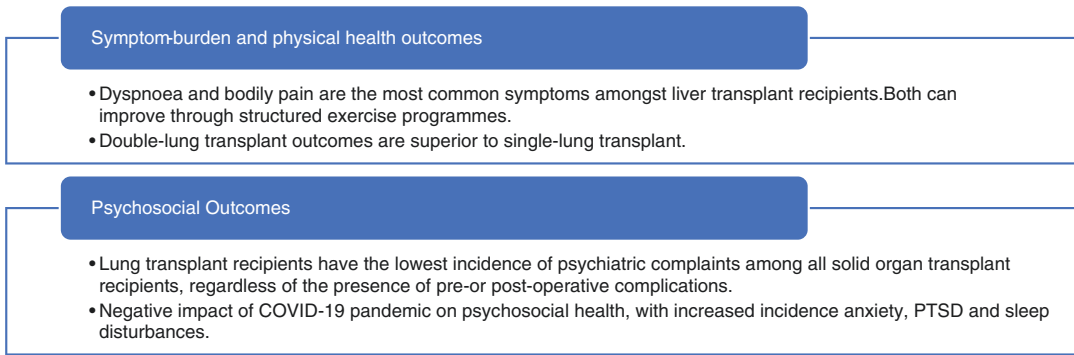


Fig. 14.7 Summary of HRQOL and PROMS after lung transplantation

Lung Transplantation

Symptom-Burden and Physical Health Outcomes After Lung Transplantation

Dyspnoea is one of the most significant limiting factors in ability to participate in physical activity after lung transplantation [171]. Nevertheless, lung transplantation has been shown to have an overall positive impact on physical functioning, with improved exercise tolerance and improved physiological parameters [172]. Structured exercise programmes after lung transplantation can systematically improve and sustain physical health outcomes [173, 174]. In addition, lung transplantation improves frailty and results in lower patient reported disability or difficulty completing daily activities due to respiratory symptom burden [175, 176].

However, energy levels are lower and bodily pain is more common in lung transplant recipients compared to healthy controls [177]. There is also evidence to suggest that long-term outcomes are superior in double-lung transplant recipients and that this is an important consideration for pre-operative patient counselling [178].

Psychosocial Outcomes After Lung Transplantation

Lung transplant recipients experience the least anxiety out of all solid organ transplant recipients, which may be related to the increased medical and psychosocial support received by this cohort [179]. Pre-transplant complications and critical illness, such as requiring extra-corporeal membrane perfusion as a bridge to transplanta-

tion do not increase the incidence of post-transplant psychological complications or depressive symptoms [180, 181]. Smith et al. [182] determined the importance of neurocognitive fitness as reduced postoperative cognition is related to mortality. Staçel et al. [183] reported that male recipients had worse overall HRQOL than female patients. The COVID-19 pandemic has had a significant influence on the psychological outcomes, resulting in a higher incidence of depression, anxiety, sleep disorders and PTSD [184, 185]. Regarding psychosocial wellbeing, the mental and somatic health was improved in patients who were pet-owners and that this did not result in an increase in atopic symptoms.

However, whilst nearly all thoracic organ transplant recipients are functionally capable of returning to work full time, many choose not to do so [186–188]. Those who choose to return to work full-time experience a significant improvement in both physical health and psychological QoL [187]. The relevant findings for this section are summarised in Fig. 14.7.

Discussion & Conclusion

The Patient-Specific Balance of HRQOL-PROMS and Its Significance for Value-Based Care in Transplantation

This chapter has examined the effects of solid organ transplantation on HRQOL & PROMS,

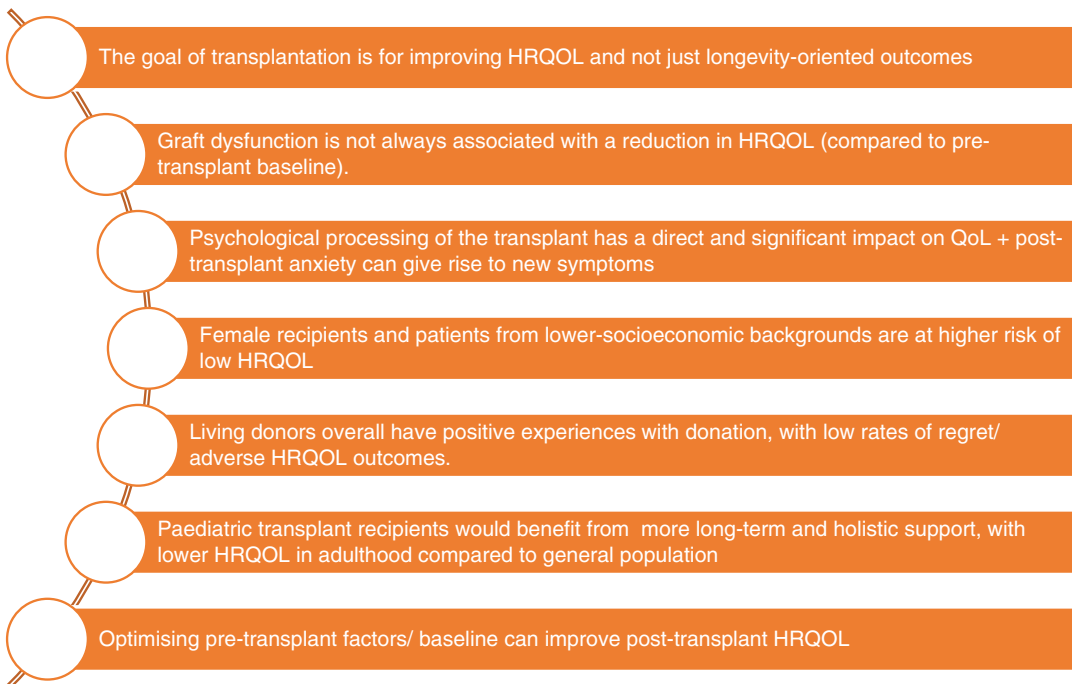


Fig. 14.8 Chapter summary- learning points for clinicians about HRQOL in transplantation

focusing specifically on patient physical health, mental health, and social well-being. Where relevant, the impact of transplantation on donors and patient families/ caregivers has also been considered. A summary for clinicians of the key conclusions from this chapter can be found in Fig. 14.8.

Overall, the quality of life of solid organ transplant recipients is comparable to that of the general population. However, across all forms of solid-organ transplantation examined in the chapter, patients who are female, non-White, former paediatric recipients and from a lower socioeconomic background are consistently at highest risk of compromised QoL after transplantation. In addition, a common theme arising in long-term QoL outcomes in paediatric transplantation is that, regardless of the type of solid-organ transplant, former-paediatric patients who survive into adulthood have lower HRQOL scores across all domains, with worse outcomes in mental health and social wellbeing, suggesting a need for close, long-term follow up.

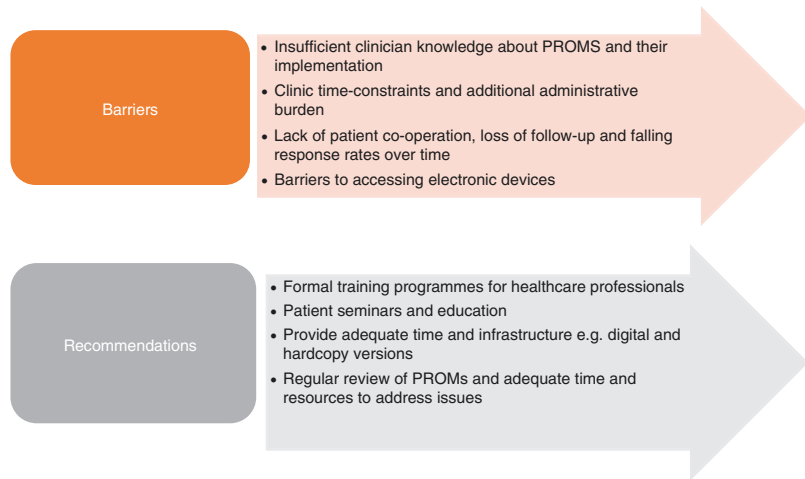
Regarding the quality of life of living donors, whilst donor outcomes are generally positive

with minimal post-operative complications, quality of life outcomes tend to be lower immediately after donation as levels of pain were greater than expected and recovery took longer than anticipated. As donation is a ‘low-risk’ surgical procedure, the quality of life of actual or potential living donors is often under investigated and such insights are underreported [189]. Nevertheless, the evidence presented in this chapter demonstrates a greater need to manage donor expectations pre-operatively through targeted information, openness and transparency. This strategy may enhance the care of prospective donors, prevent long-term sequelae from the donation process and potentially, improve donation rates. In addition, the routine HRQOL-PROMs data collection has the potential to reduce the underdiagnosis and undertreatment of new and disease-related symptoms [190].

These examples allow us to appreciate that physical, mental and social HRQOL components must be considered not as independent variables, but existing in relation to each other in a precarious, patient-specific balance [191]. As a result, a

Fig. 14.9

Implementation of HRQOL/PROMS in clinical care pathways



deficit in one domain results in downstream effects on the other variables. This balance is maintained by internal factors, such as unique patient psycho-social characteristics (e.g. demographics, comorbidities, personality type, social networks) and external, medical and transplant-related variables (e.g. comorbidities, graft conditions, presence of post-operative complications etc.) [190] (Figs. 14.7 and 14.8).

For instance, several studies presented in this chapter have demonstrated that transplantation has a positive impact on recipient physical health, fitness and energy levels and that more active patients report greater wellbeing. Nevertheless, few patients increase their level of physical activity despite being capable of doing so. There may be several reasons for this, including anxiety about graft failure, persistent chronic fatigue, or a lack of structured exercise support programmes available to maintain initial improvements in somatic health.

Using the above principles, it is possible to use HRQOL—PROMS data to unravel the problem systematically e.g. thorough baseline physical health assessments help identify groups of patients (e.g. frail, elderly, obese, female and non-White) who may require more support in regaining physical function after transplantation. Subsequently, HRQOL-PROMS data in transplant recipients allows us to appreciate that mental health problems are typically related to problematic psychological processing of the

transplant and there is a higher incidence among certain personality types, such as anxious avoidant or introverted. Understanding these ‘patient types’ allows healthcare providers to deliver relevant, valuable, personalised post-transplant care in a more clinically beneficial and cost-efficient way [192] (Fig. 14.9).

In addition, such HRQOL data can help to optimise recipient preparation, by identifying at an early-stage individuals who are at risk of adverse QoL outcomes after transplantation. In turn, this can help to optimise the benefits of transplantation on patient HRQOL starting with addressing waiting list dynamics and helping to establish a balance between risk-benefit evaluations and ‘justice’ in the allocation of the finite organs available for transplantation [193].

On a larger scale, HRQOL-PROMS have the potential to improve doctor-patient collaboration, by generating an ongoing, open dialogue between the key ‘stakeholders’ (Fig. 14.10). Measuring QoL at regular intervals allows patients to monitor their own progress over time and encourage health literacy and positive self-management [194]. At the highest level, this data can be used to make pivotal decisions about clinical pathways, policy, and resource allocation, by allowing for accurate cost-benefit analysis and facilitating the implementation of a ‘values-based medicine’ approach into everyday clinical practice [195].

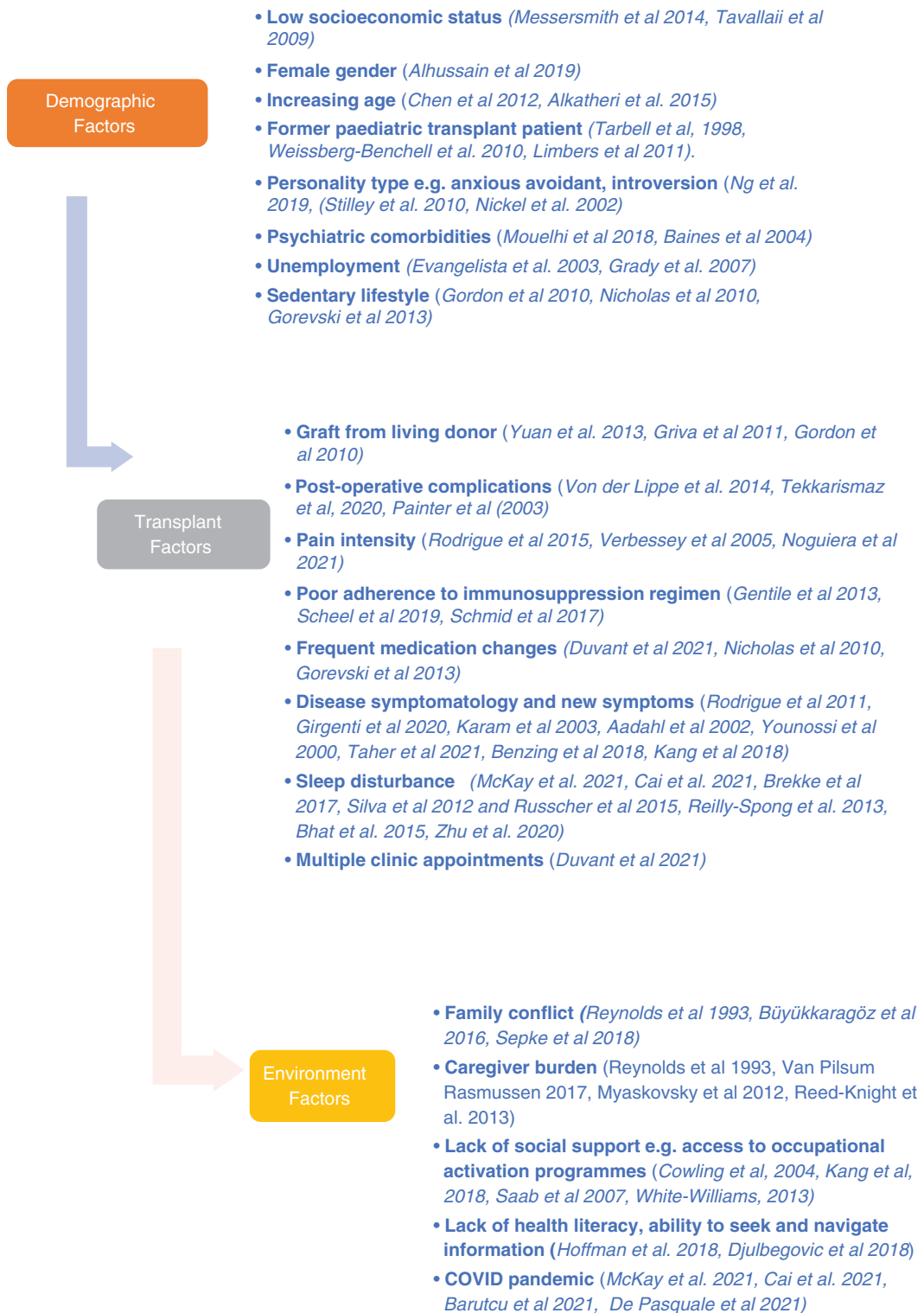


Fig. 14.10 Predictors of impaired quality of life after transplantation

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