

IN THE NAME OF GOD

REHABILITATION FOR SOLID ORGAN TRANSPLANTATION

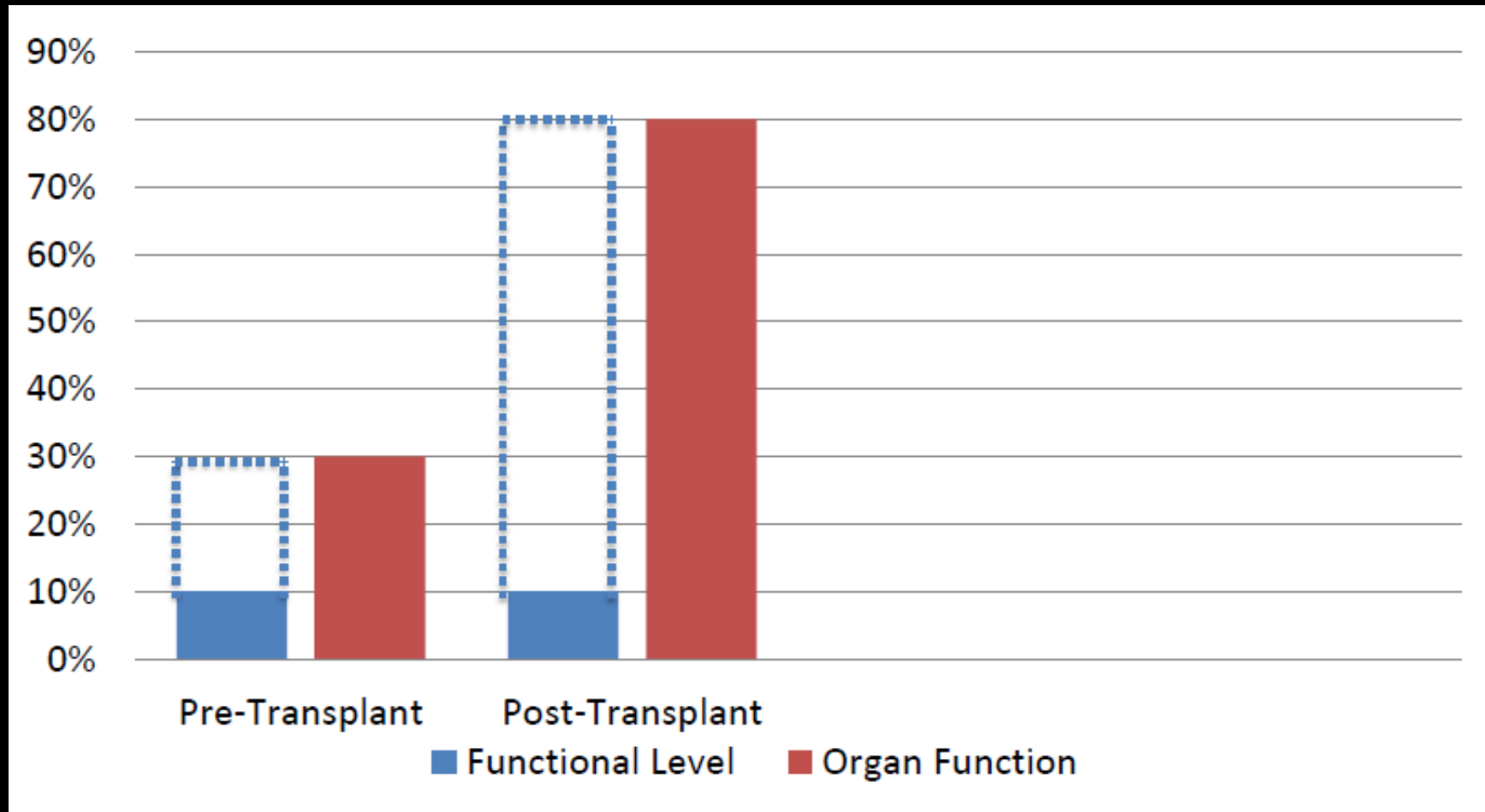
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- Solid organ transplantation
 - Gold-standard treatment for many with end-organ failure
 - Can offer a new independence from the burden of disease
- However solid organ transplant recipients (SOTRs) remain at:
 - High risk of cardiovascular disease
 - Poor quality of life and physical functioning

Functional Level versus Organ Function



Main Components of Rehabilitation Program

- PATIENT ASSESSMENT
- EDUCATION AND SELF-MANAGEMENT
- PSYCHOSOCIAL CARE AND SUPPORT
- NUTRITIONAL INTERVENTION
- PHYSICAL THERAPY AND EXERCISE TRAINING

PATIENT ASSESSMENT

CardioPulmonary Exercise Test(CPET)

- Pre-operative cardiopulmonary exercise testing is used to objectively measure physical fitness before major surgery.
- Fitness predicts post-operative complications and death



- Recently cardiopulmonary exercise testing (CPX-to measure maximal oxygen consumption) has been increasingly used to
 - Establish the prognosis in patients with severe heart failure
 - Define indications to heart transplantation.
- The measurement of oxygen uptake and anaerobic threshold during exercise is an objective, reproducible, safe and non-invasive method to assess cardiac reserve.
- Thus, the parameter may be useful
 - Not only in defining the indications,
 - But also in the monitoring the patient's clinical state and timing of heart transplantation.

Nessler J, Piwowarska W. [Clinical usefulness of cardiopulmonary exercise testing in patients with cardiac failure waiting heart transplantation]. Przegląd lekarski. 1997;54(11):819-21.

II. Indications for Cardiopulmonary Exercise Testing

Idelle M. Weisman, Darcy Marciniuk, Fernando J. Martinez,
Frank Sciurba, Darryl Sue, Jonathan Myers

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- Prediction of post-operative morbidity/survival in persons undergoing major surgery:

- Abdominal aortic aneurysm repair
- Colorectal surgery
- **Hepatic transplant** and resection surgery
- Pancreatic surgery
- **Renal transplant**,
- Upper gastro-intestinal surgery



AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0825 Cardiopulmonary
Exercise Testing

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania
Updated 04/2017

- Exercise intolerance is an important comorbidity in patients with CKD.
- Anaerobic threshold (AT) determines the upper limits of aerobic exercise and is a measure of cardiovascular reserve.
- Using cardiopulmonary exercise testing, cardiovascular reserve was evaluated in 240 patients who were waitlisted for kidney transplantation between 2008 and 2010, and patients were followed for ≤ 5 years.
- According to Kaplan-Meier estimates, patients with AT $< 40\%$ of predicted peak VO_2 had a significantly reduced 5-year cumulative overall survival rate compared with those with AT $\geq 40\%$ ($P < 0.001$).

Functional cardiovascular reserve predicts survival pre-kidney and post-kidney transplantation{Ting, 2014, Journal of the American Society of Nephrology}

- Patient's listed for liver transplant have significant functional limitations, with a weighted mean VO2 below the threshold level required for independent living.
- The studies support **CPET** as an objective and independent predictor of pre- and post-transplant mortality.

Ney M, Haykowsky MJ, Vandermeer B, Shah A, Ow M, Tandon P. Systematic review: pre- and post-operative prognostic value of cardiopulmonary exercise testing in liver transplant candidates. *Alimentary pharmacology & therapeutics*. 2016;44(8):796-806.

Main Components of Rehabilitation Program

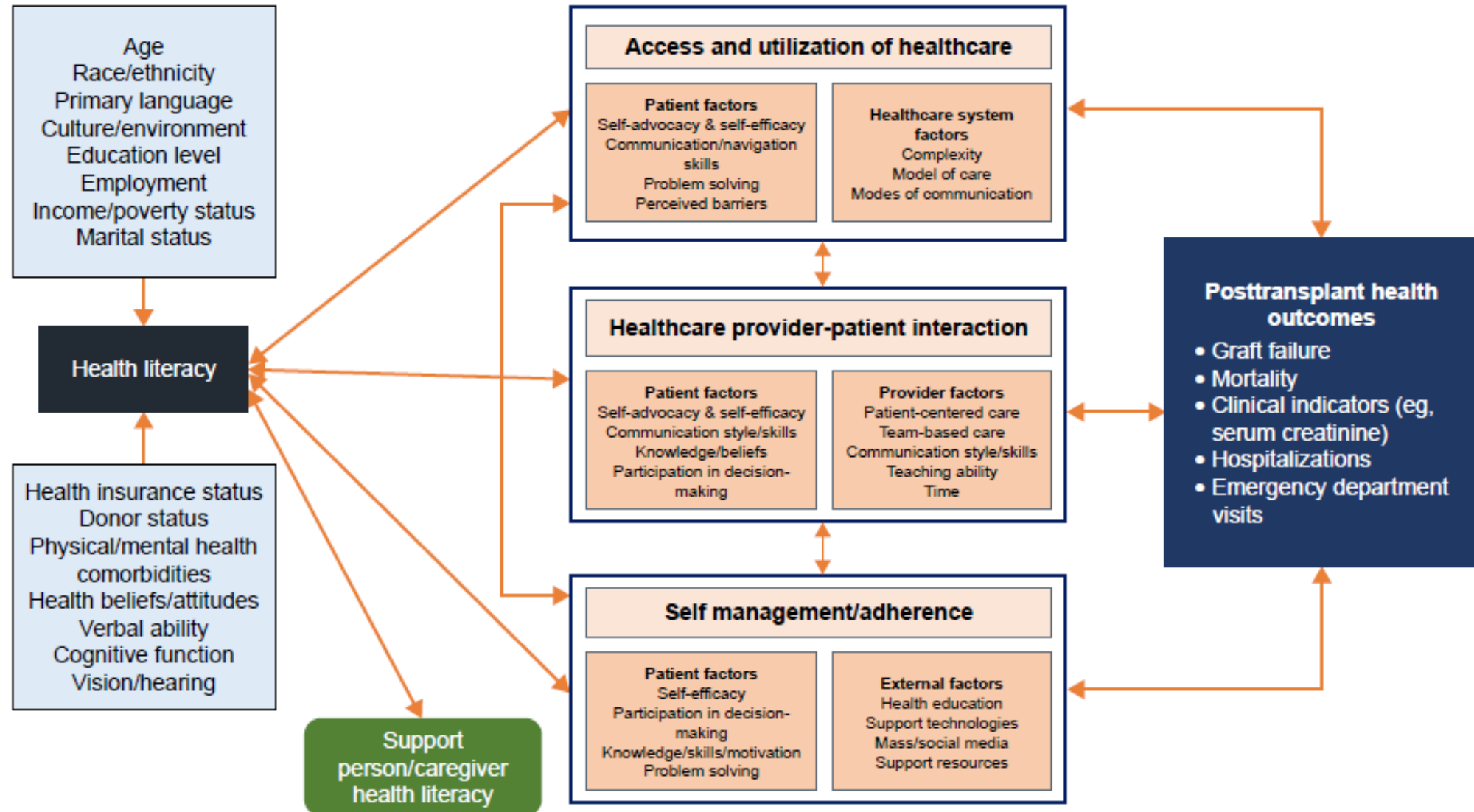
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EDUCATION AND SELF-MANAGEMENT

- Optimizing wellness and health are the most critical goals for patients post solid-organ transplantation.
- Low health literacy has important implications for wellness and health, increasing patient risk for negative health outcomes.
- More than 30% of the general US patient population has low health literacy.

Health literacy in solid-organ transplantation: a model to improve understanding, Patient Preference and Adherence 2018;12 2325–2338

The Health Literacy Model in Transplantation (HeaL-T)



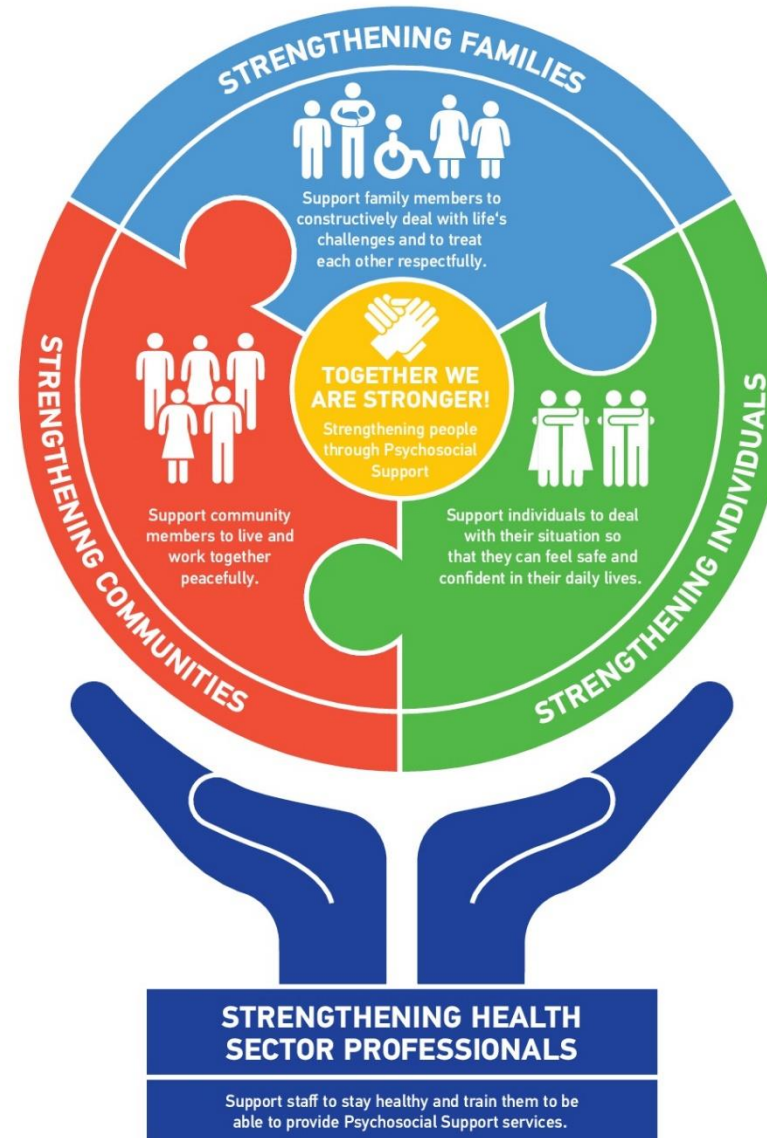
Low health literacy is associated with

- Older age
- Lower education level
- Unemployed
- Lower income/living in poverty
- Public or no health insurance statusa
- Minority race/ethnicity
- Primary language other than English
- Cultural/environmental challengesa
- Not married
- Poorer physical/mental health
- Increased comorbidities
- Negative health beliefs/attitudesa
- Limited cognitive function
- Deceased donor
- Limited verbal abilitya
- Increased vision/hearing impairmentsa

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WHAT IS PSYCHOSOCIAL SUPPORT?



- **Poor psychological adjustment** to organ transplantation appears to be a major contributor to
 - Reduced quality of life
 - Increased physical morbidity.
- **191 heart transplant recipients** in a prospective examination of the prevalence, clinical characteristics, and risk factors for DSM-III-R disease during the **3 years postsurgery**.
- Survival analysis indicates that cumulative risks for disorder onset were:
 - **MDD**, 25.5%; **adjustment disorders**, 20.8% (17.7% with **anxious mood**); **PTSD-T**, 17.0%; and any assessed disorder, 38.3%. There was only one case of **GAD**.

- Factors increasing cumulative risk for psychiatric disorder posttransplant included:
 - Pretransplant psychiatric history
 - Female gender
 - Longer hospitalization
 - More impaired physical functional status in the perioperative period
 - Lower social supports from caregiver and family in the perioperative period.

- There was broad based multidisciplinary support for proactive **pretransplant screening** to discern individual psychosocial needs; focused:
 - **Pretransplant interventions** to improve candidacy and future compliance;
 - **Posttransplant programs** that address psychosocial, rehabilitation, and financial issues.
- Among psychosocial providers of solid organ transplantation services, there is support for **expanding routine screening and support services** to individuals who are candidates for and undergo solid organ transplantation.

Approaching a consensus: psychosocial support services for solid organ transplantation programs
{Skotzko, 2001, Prog Transplant}

- Despite conflicting conclusions, the larger prospective studies in both renal and liver transplantation show that:
 - Depression is an independent risk factor of overall mortality and, in some studies, infection and malignancy.
- All patients should be screened for depression
- Psychiatric disease that occurs after transplantation is a greater predictor of morbidity and mortality than disease before transplantation, but long-term follow-up (>5 years) is lacking.
- There is no justification for excluding patients from transplantation based on a mental health diagnosis if the patient's illness is well controlled and adequate social support is in place.

- 22 studies (10 heart, total n = 1738; 6 liver, n = 1063; 5 kidney, n = 49515; 4 lung, n = 584; 1 pancreas, n = 80; 1 mixed recipient sample, n = 205) were identified.
- In each, depression and/or anxiety were typically measured before or early after transplantation. Follow-up for outcomes was a median of 5.8 years (range, 0.50-18.0).
- Depression **increased the relative risk (RR) of mortality** by 65%
- Risk was unaffected by type of transplant or other study characteristics.
- Depression **increased death-censored graft loss risk**.
- **Anxiety** did not significantly increase mortality or morbidity risks (assessed in single studies).
- **Depression screening and treatment may be warranted**, although whether these activities would reduce posttransplant mortality requires study.

- Meta-analyses have shown that post-organ transplantation quality of life improves for social, physical and daily activity functioning, **but not consistently for psychological health.**
- Psychiatrists can play a useful role:
 - **not only in selecting the best suitable candidate** for the procedure by psychosocial screening
 - **but also to tackle post-operation psychological issues** that trouble patients as well as caretakers and decrease their quality of life.

Main Components of Rehabilitation Program

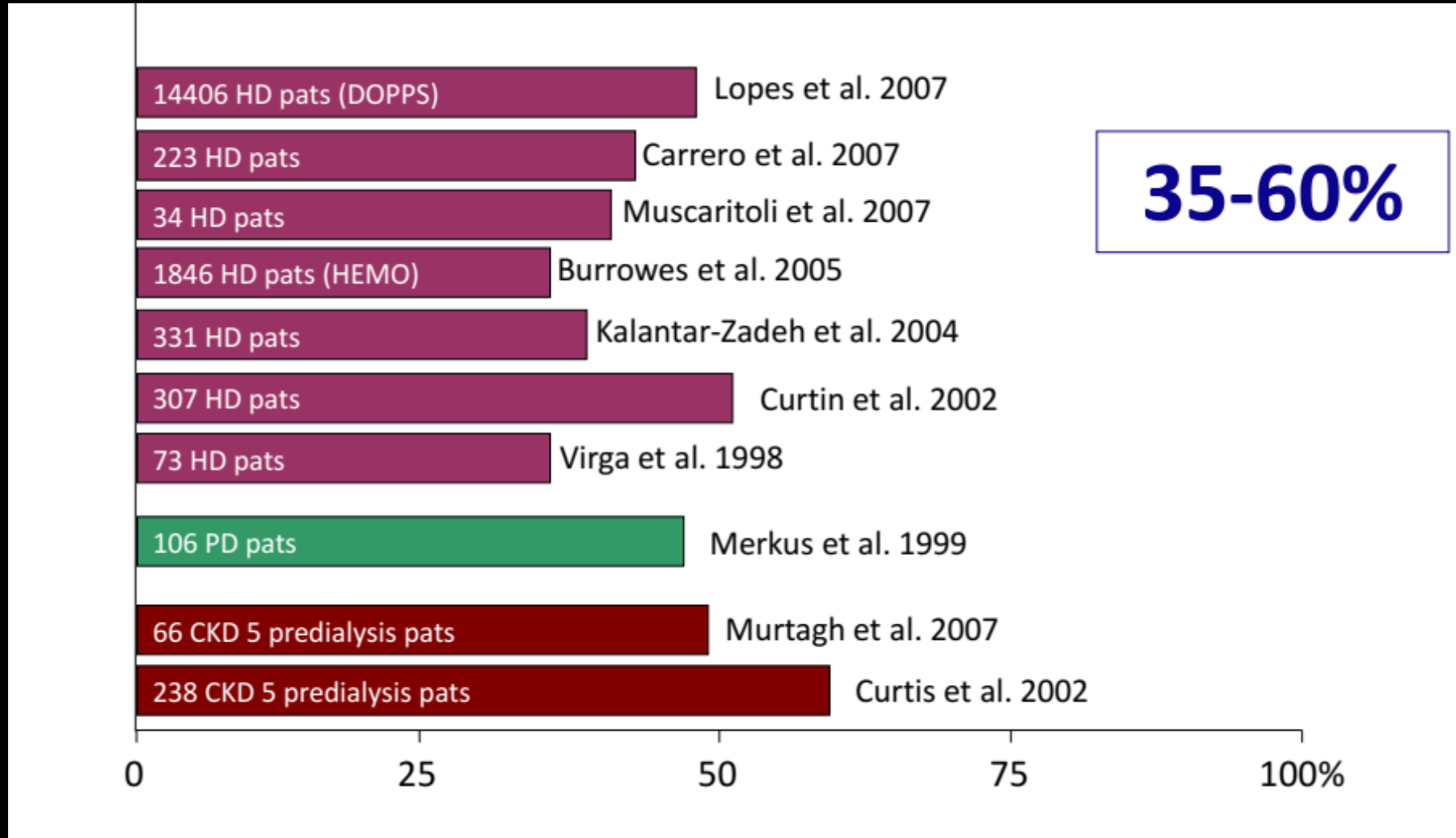
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NUTRITIONAL INTERVENTION

- Timely nutrition assessment and intervention in organ transplant recipients may improve outcomes surrounding transplantation.
- Malnutrition compromises posttransplant survival
- Prolonged waiting times worsen outcomes when patients are already malnourished.
- Severe obesity may decrease graft function and survival in kidney transplant recipients.
- In the pretransplant phase, nutritional goals include
 - Optimization of nutritional status
 - Treatment of nutrition-related symptoms induced by organ failure.

- During the acute posttransplant phase, adequate nutrition is required to
 - Help prevent infection,
 - Promote wound healing,
 - Support metabolic demands,
 - Replenish lost stores,
 - Perhaps mediate the immune response.
 - Nutrient recommendations reflect posttransplant metabolic changes.
- Organ transplantation complications including rejection, infection, wound healing, renal insufficiency, hyperglycemia, and surgical complications require specific nutritional requirements and therapies.

Prevalence of malnutrition in patients with chronic renal failure



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PHYSICAL THERAPY AND EXERCISE TRAINING

- Many patients who require transplant have chronic diseases pre-operatively leading to:
 - Muscle weakness
 - Possible prolonged hospitalization
 - Fatigue
 - Extended confinement to bed, room, or house
 - Poor ambulatory skill
 - Poor breathing mechanics
 - Inability to adequately clear pulmonary secretions
- ***Therefore.....***

Physical Therapy is consulted for.....balance abnormalities, weakness, poor endurance, poor flexibility and decreased range of motion, fall risk, loss of independent ambulation, poor bed mobility, inability to perform transfers, skin breakdown, edema, breathing re-training, airway clearance, etc.

- Post-operatively, patients may experience:
 - Weakness
 - Possible prolonged hospitalization
 - Fatigue
 - Extended confinement to bed, room, or house
 - Poor ambulatory skill
 - Poor breathing mechanics
 - Inability to adequately clear pulmonary secretions
- ***Therefore.....***

Physical Therapy is consulted for....balance abnormalities, weakness, poor endurance, poor flexibility and decreased range of motion, fall risk, loss of independent ambulation, poor bed mobility, inability to perform transfers, skin breakdown, edema, breathing re-training, airway clearance, etc.

REHABILITATION FOR SOLID ORGAN TRANSPLANTATION

1. Physical Therapy for Outpatient Treatment, Pre-Transplant
2. Physical Therapy for the hospitalized(Inpatient) pre-transplant patient
3. Physical Therapy for the hospitalized(Inpatient) post-transplant patient
4. Physical Therapy for Outpatient Treatment, Post-Transplant

Physical Therapy Considerations for Outpatient Treatment, Pre- and Post-Transplant

Limitations of Transplant Candidates and Recipients

- **Reduced exercise and functional capacity**
- Decreased health-related quality of life
- Weakness
- Muscle atrophy
- Decreased bone density
- Increased fatigue
- Decreased cardiopulmonary capacity of 40-60%
- Psychosocial factors

Exercise and the Peri-Op Patient

- Increased work & exercise capacity
- Maximize muscle strength and endurance
 - Improved muscle efficiency
- Improved psychosocial factors such as anxiety and depression
 - Maximize quality of life

Goals for the Patient Pre-Transplant

- Preserve muscle strength and endurance:
 - Focus on proximal muscle groups to counteract effects of corticosteroids
 - Decreased mobility expected as inpatient,
 - Preserve UE/LE function,
 - Improve breathing mechanics
- Maximize functional abilities
- Educate patient on:
 - What to expect post transplant
 - Signs and symptoms of rejection
 - Osteoporosis prevention
 - Co-morbidities such as diabetes

Physical Therapy for the hospitalized pre-transplant patient: Implications and Considerations

Components of the Physical Therapy Inpatient Evaluation

- Social situation
- Vital signs/Lab values
 - Working with physicians for approved ranges for PT to work within as many of these patients can be highly atypical (Platelet, INR levels, BP ranges, O2 levels, HR, etc.)
- Strength
- ROM
- Aerobic capacity (6-min walk, 10m walk, etc.)
- Functional mobility
- Balance
- Compliance with HEP
- Discharge recommendations
 - Is inpatient rehab more appropriate pre-transplant before starting immunosuppression and lifting restrictions?
 - What are their financial rehab benefits?

Goals of Pre-operative Inpatient Physical Therapy

- Patients to receive transplants are in the majority of cases chronically ill and the range of physical recovery in the presence of organ failure is highly variable based on the progression of their disease.
- PTs work to :
 - Optimize aerobic capacity
 - Maximize musculoskeletal strength
 - Maximize functional endurance
 - Maximize and maintain functional independence
 - Exercise education to form good habits for post-operative recovery to optimize outcomes
 - Making sure patients are independent with a HEP to continue addressing goals after D/C
 - Education about post-operative activity requirements and expectations to reduce anxiety and increase post-operative compliance
 - Make disposition recommendations to allow patients to meet above goals

Barriers to Inpatient PT progression

- Acuity of illness
 - Medical status
 - Cognitive status
- ICU ventilation and sedation
- Line placement (can vary by facility)
- Lab values and vital signs outside treatable ranges
 - Instability of vital signs
 - Abnormal responses to exercise
- Inpatient testing and procedures
- Patient compliance

Physical Therapy for the hospitalized post-transplant patient: Implications and Considerations

Post-Operative Care in the ICU

- Evaluation
 - Vitals
 - ROM/strength
 - Skin/wound assessment
 - Posture assessment
 - Pulmonary assessment
 - Endurance/activity tolerance
 - Functional mobility

Post-Operative Care in the ICU

- Interventions
 - Focus on impaired gas exchange
 - Airway clearance
 - Positioning
 - Therapeutic exercise
 - Transfer training
 - Gait training

Post-Operative Goals

- Optimizing pulmonary hygiene and chest wall mobility to wean from ventilator and supplemental oxygen
- Improve strength and ROM
- Improve exercise tolerance through low to moderate intensity exercise and ADLs

After the ICU

- Increasing MET level
 - Focus on independence of ADLs
 - Increase endurance
 - Progression of exercises and guidelines for termination of exercise
 - Preparing for discharge
 - Patient education
-
- **Home exercise program**

Therapy Considerations for Heart Transplantation

- Pre-transplant, patients will have greatly reduced exercise tolerance due to decreased cardiac output
- Sternal precautions
- Denervation of the heart
 - Importance of warm-up and cool-down
 - Use of RPE scale to monitor exercise intensity
- Close monitoring of vital signs before, during, and after exercise

Therapy Considerations for Lung Transplantation

- CO₂ retention
- Pulmonary hypertension precautions
- Incisional precautions
- Breathing re-training
- Airway clearance
- Postural considerations

Therapy Considerations for Liver Transplantation

- Complications from cardiopulmonary bypass
- Pulmonary involvement
- Central nervous system complications
- Abdominal scar can contribute to poor posture
- May also exhibit poor balance, coordination, endurance
- Energy conservation education

Therapy Considerations for Kidney Transplantation

- Effects of exercise on blood glucose control
- Increased incidence of cardiovascular disorders, HTN, dyslipidemia, cancer, osteoporosis
- Close monitoring of vital signs, particularly BP, prior to and during exercise
- Resistive exercises and osteoporosis precautions
- Increased incidence of tendon injuries, especially Achilles

Kidney Transplant



- This study included **263 patients**, consecutively referred **over a 4-year period**, to a pragmatic 12-week renal rehabilitation (RR) programme delivered within a **National Health Service (NHS)**.
- There were significant improvements in:
 - **physical function**
 - exercise capacity
 - functional ability
 - **mental well-being**
 - anxiety
 - depressionin the 77 patients who completed the RR programme.
- Compliance/adherence data indicate that this type of rehabilitation programme is particularly well received **by pre-dialysis (PD) CKD** and **post-transplantation patients**.

Evaluation of a pragmatic exercise rehabilitation programme in chronic kidney disease {Greenwood, 2012, Nephrol Dial Transplant}

- **757 patients** (male 54%) (242 haemodialysis patients, 221 kidney transplant recipients, 43 peritoneal dialysis patients, 251 non-dialysis CKD patients) were referred for RR between 2005 and 2017.
- There is an association between
 - Completion of an RR programme,
 - RR success,
 - Lower risk of a combined event
- RR interventions to improve exercise capacity in patients with CKD **may reduce risk of morbidity and mortality,**
- '**Non-completers**' of RR had a **1.6-fold greater risk** of a combined event

Mortality and morbidity following exercise-based renal rehabilitation in patients with chronic kidney disease: the effect of programme completion and change in exercise capacity{Greenwood, 2018 Nephrol Dial Transplant}

- The most active KTRs engaged in more intentional exercise.
- Lower levels of PA were positively associated with more CVD risk factors.
- Higher PA levels were associated with
 - Younger age
 - More positive KTR outcomes

- In adult kidney transplant patients, a structured physical exercise program improved:
 - Aerobic capacity
 - Ameliorated muscle performance
 - Quality of life.
- Exercise intervention had **no clinically relevant impact on anaemia, glycaemia or lipidaemia.**
- In contrast, exercise training **improved several aspects of quality of life.**
- **No harms** were observed in the short-term, but long-term RCTs are required.
- Overall, in mid-age kidney transplant patients without major comorbidities, an aerobic or resistance supervised exercise **lasting 3-6 months** could be suggested within the comprehensive treatment of kidney transplant.

- For kidney transplant recipients, supervised exercise training was shown to significantly **improve VO2 peak and QOL.**
- However, exercise training **did not improve allograft kidney function.**

The efficacy of exercise training in kidney transplant recipients: a meta-analysis and systematic review {Oguchi, 2018, Clinical and experimental nephrology}

- The new method incorporates 3 major components:
 - Physical exercise,
 - Behavioral interventions,
 - Nutritional guidance.
- RESULTS:
 - The adherence to training and follow-up was 100% in the intervention group, compared with 25% at 12 months in the control group.
 - There was a trend for a higher glomerular filtration rate in the intervention group
 - The quality of life (SF-36) mean score improved more in the intervention group
 - There was a significantly higher employment rate in the intervention group,

- Although the research evidence base needs enriching,
- The association between exercise and better outcomes in the dialysis population is **sufficiently strong** to state the following.



INTRA-DIALYTIC EXERCISE TRAINING: A PRAGMATIC APPROACH, 2014 European Dialysis and Transplant Nurses Association/European Renal Care Association

Heart Transplant



- One of the most important prognostic factors in heart failure patients is physical capacity.
- Patients with very poor physical performance and otherwise eligible, may be listed as candidates for heart transplantation (HTx).
- After such surgery, life-long immunosuppression therapy is needed to prevent rejection of the new heart. The dark side of immunosuppression is the increased risk of infections, kidney failure, cancer and advanced atherosclerosis (cardiac allograft vasculopathy),

- Poor aerobic capacity prior to graft deterioration is not only limited to the failing heart, but also caused by peripheral factors, such as limited function in the skeletal muscles and in the blood vessels walls.
- Exercise rehabilitation after HTx is of major importance in order to improve physical capacity and prognosis.
- In short, this article demonstrates a strong association between physical capacity measured after HTx and long-term survival.

- An 8-week supervised exercise program was observed to improve
 - Functional capacity,
 - PFT,
 - QOL,
 - Depressionamong patients who had HF, HTx, or LVAD.
- **Supervised exercise** should be recommended for every patient included in a heart transplant program.

Efficacy of the cardiac rehabilitation program in patients with end-stage heart failure, heart transplant patients, and left ventricular assist device recipients{Karapolat, 2013, Transplant Proc}

- We found moderate quality evidence suggesting that
 - Exercise-based cardiac rehabilitation **improves exercise capacity**, and that
 - Exercise has no impact on health-related quality of life in the short-term (median 12 weeks follow-up),
- Cardiac rehabilitation appears **to be safe** in this population

Exercise-based cardiac rehabilitation in heart transplant recipients Rev{Anderson, 2017, The Cochrane database of systematic reviews}

Liver Transplant



- Clinical trials addressing the usefulness of exercise in patients with cirrhosis have shown that it improves:
 - Metabolic syndrome, sarcopenia, physical fitness/cardiopulmonary endurance , health-related quality of life, and hepatic venous pressure gradient.
- We believe that an exercise program coupled to a nutritional intervention
 - benefits both cardiopulmonary and musculoskeletal functions, ultimately translating into improved functional status, sense of well-being, and possibly less complications from portal hypertension.

Exercise and physical activity for patients with end-stage liver disease: Improving functional status and sarcopenia while on the transplant waiting list{Duarte-Rojo, 2018, Liver Transpl}

- In conclusion, although supervised exercise training is the prevailing approach to manage ESLD patients, such intervention **is not sustainable or feasible for most patients.**
- Innovative **home-based physical activity** interventions may be able to effectively reach a larger number of patients.

- **Fatigue** is a chronic problem in liver transplant recipients and may influence daily functioning and health-related quality of life (HRQoL).
- 18 fatigued liver transplant recipients (mean age 51 years, 10 men/8 women) participated in a 12-week rehabilitation programme, which included supervised exercise training and daily physical activity counselling.
- After the programme, patients showed improvements in:
 - Daily functioning
 - Participation domain 'autonomy outdoors'
 - HRQoL domains 'physical functioning'
 - Anxiety and depression were unchanged post-programme.

- Supervised (SE) and home-based exercise (HBE) training regimes are effective on reconditioning patients with (FAP) after liver transplantation, but research of the long-term retention of the benefits attained in patients with FAP has not yet been conducted.
- In this 5-year follow-up study, we aimed to determine whether the exercise training gains in body composition, physical activity, and function promoted by a 24-week SE or HBE training regimes are retained in 16 patients with FAP who resume normal activity.
- Long-term resumption of normal activity following a 24-week SE or HBE regime in patients with FAP resulted in loss of exercise induced
 - increases in physical activity but counterweighted postoperative losses in femoral bone mineral density
 - substantially retained the benefits in walking capacity, muscle mass, and quality, in particular, in the SE group.

Lung Transplant



- Physical rehabilitation of lung transplant candidates and recipients plays an important in
 - Optimizing physical function prior to transplant
 - Facilitating recovery of function post-transplant.
- As medical and surgical interventions in lung transplantation have evolved over time, there has been a demographic shift of individuals undergoing lung transplantation including **older individuals**, those with **multiple co-morbidities**, and **candidates with respiratory failure** requiring bridging to transplantation.
- Rehabilitation focuses on
 - Functional assessment
 - Exercise prescription
 - during an uncomplicated and complicated clinical course in the pre-transplant, early and late post-transplant periods.

- Pulmonary rehabilitation programme including aerobic exercise training and/or resistance exercise training.
-
- **PRIMARY AND SECONDARY OUTCOMES:**
 - **Primary outcomes:** Quality of life and exercise capacity
 - **Secondary outcomes:** Survival rate after transplant surgery; pulmonary function; respiratory muscle strength; psychological aspects; upper and lower extremity muscle strength and adverse effects.
- PR is an effective treatment option for patients on the waiting list for lung transplantation and can improve quality of life and exercise capacity in those patients.

- This review explores the benefits of structured exercise programs on the health of SOTRs.
- Incorporation of exercise into the routine post-operative care of transplant recipients should be strongly considered due to the improvement in many aspects of wellbeing in these patients and the absence of significant complications or side-effects.



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