

PRO Gap Analysis in Antibody Mediated Rejection, Delayed Graft Function, Lupus Nephritis, and Membranous Nephropathy

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Key Findings

- Well developed and validated Patient-Reported Outcomes (PRO) instruments in Lupus Nephritis (LN): **LupusPRO**.
- There are no disease-specific instruments for Antibody Mediated Rejection (AMR), Delayed Graft Function (DGF), and Membranous Nephropathy (MN).

Conclusions

Disease-specific PROs should be developed in AMR, DGF and MN to allow for granularity in measuring impact of disease and treatment from a patient-centered perspective in clinical trials. Impacts related to anxiety/depression and social functioning could be areas for further investigation.

Background and Objectives

Nephrology conditions such as AMR, DGF, LN, and MN have a known impact on patients’ quality of life that should be considered when measuring treatment benefit from patients’ perspectives. This desk research aimed to develop Patient-Reported Outcome (PRO) strategies for drug clinical development in AMR, DGF, LN, and MN.

Methods

I. Targeted Literature Review:

- Research performed in:
- Medline and PsycInfo** for **qualitative studies** published before July 2023 ➔ **7 references selected**
 - Medline** for PRO instruments used in **published studies** in the 10 years before June 2023 ➔ **41 references selected**
 - CT.gov** for PRO instruments used in **registered studies** in the 5 years before June 2023 ➔ **21 references selected**
 - PROQOLID™** database for **PROs developed in nephrology** in July 2023 ➔ **45 PRO selected**
 - PROINSIGHT™** database and Google and PubMed for **guidelines** in July 2023 ➔ **1 guideline selected**
 - No PRO claim was identified** in the **PROLABELS™** database for any of the 4 therapeutic indications

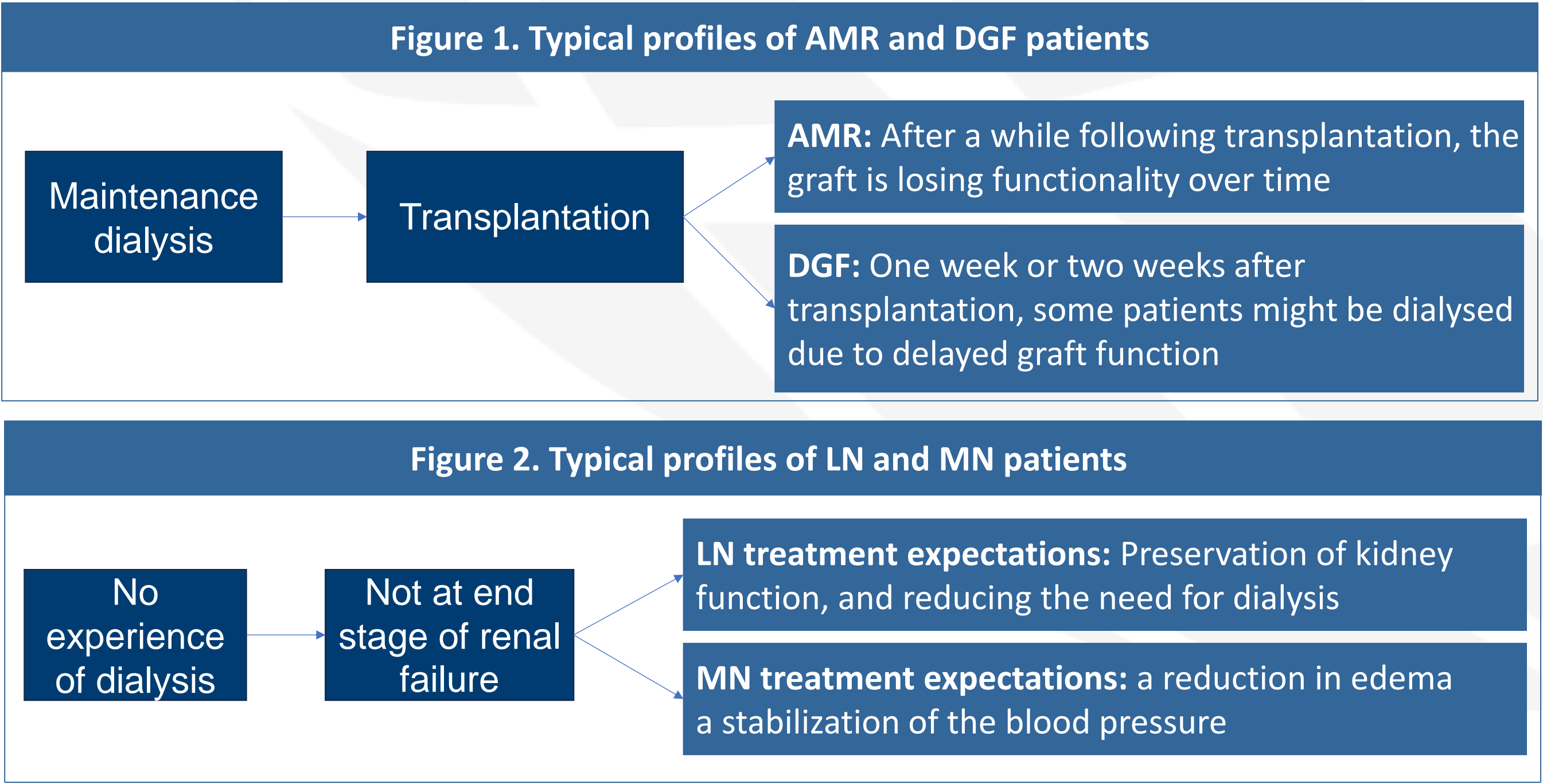
II. Gap Analysis:

- Based on the targeted literature review results & the review of a total of 10 questionnaires.
- Concept mapping** was performed by reviewing the item content of each PRO as compared to the conceptual model to assess the relevance and adequacy of the PROs for the targeted patient population and identify any important gaps in terms of conceptual coverage.
- Appraisal of **psychometric properties** of 10 selected PROs.
- The **strengths and weaknesses** of each PRO were identified in terms of development methods, content and psychometrics.

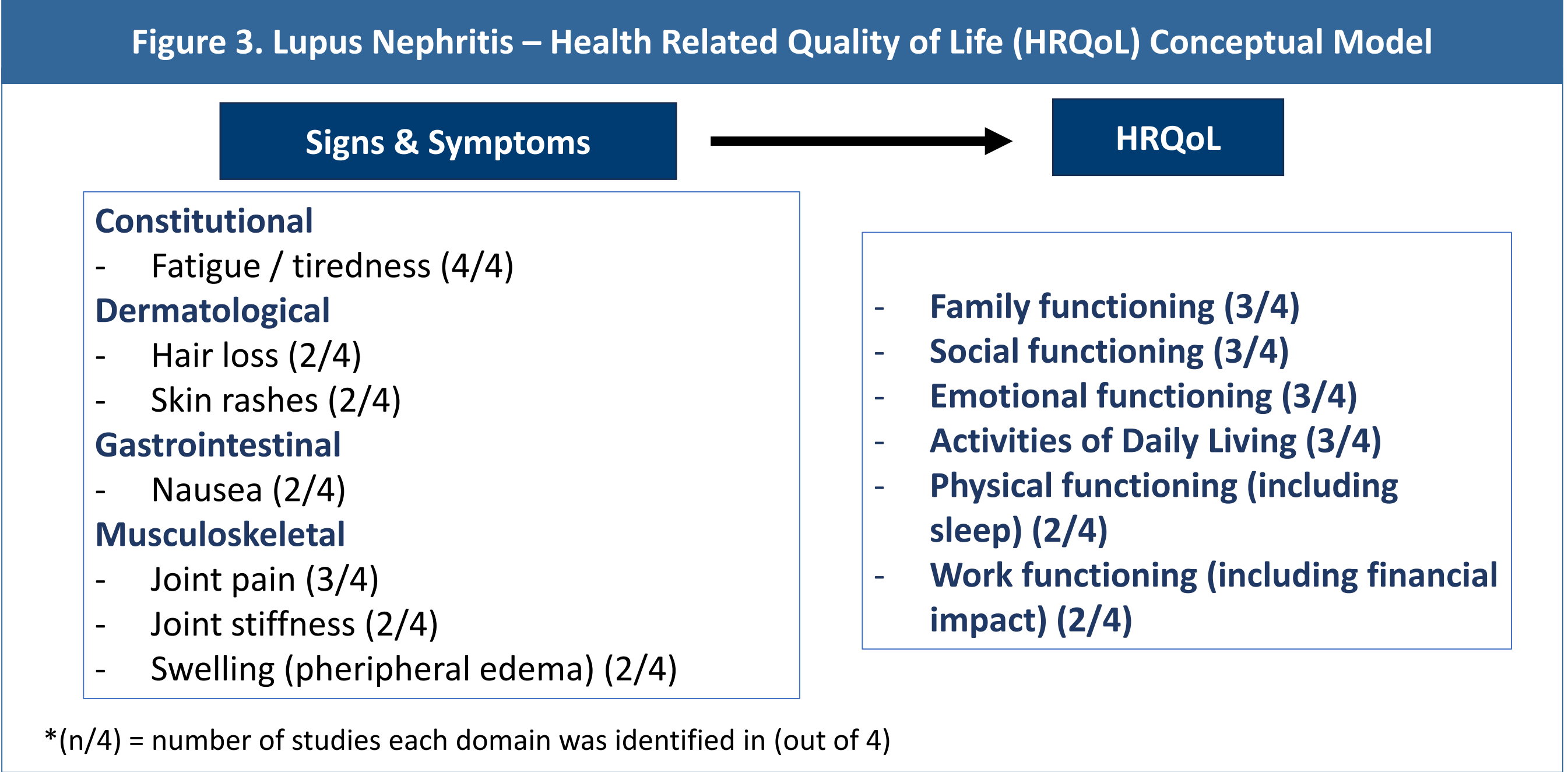
Results

I. Concepts with an impact on Health-Related Quality of Life

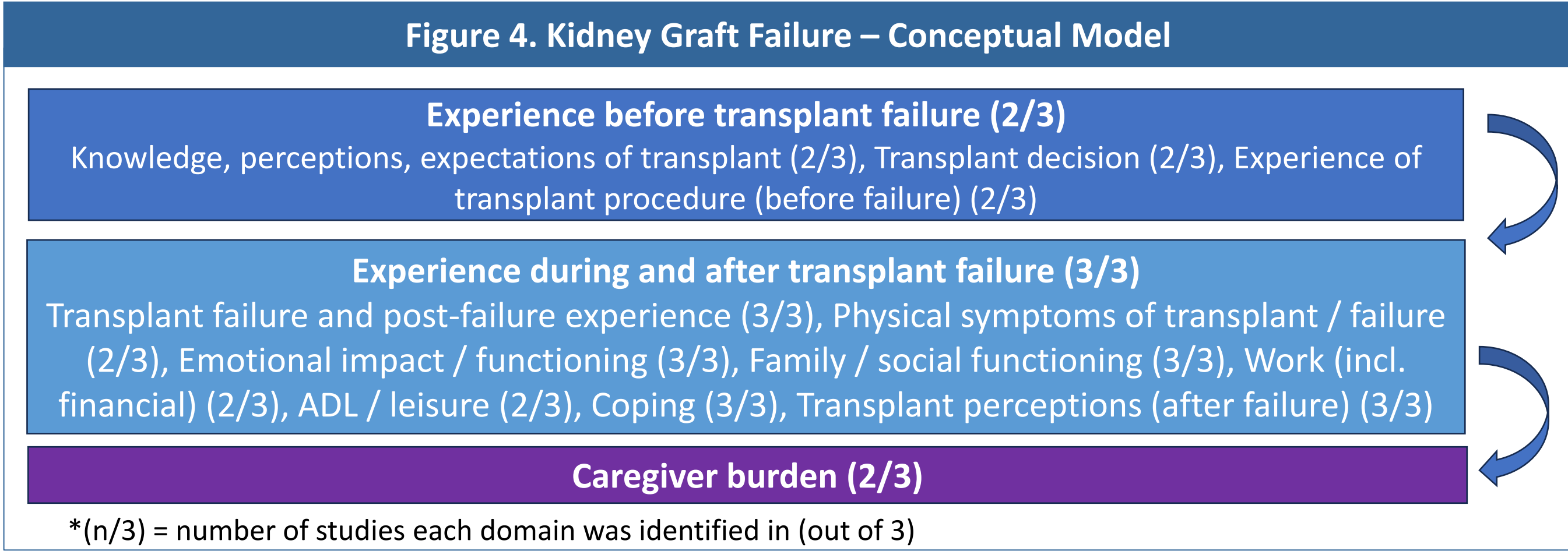
The typical profiles of AMR, DGF, LN and MN patients are shown in Figure 1 and 2.



In the 4 studies analyzed, several signs and symptoms impacting the Health-Related Quality of Life of patients with LN, were identified. Signs and Symptoms that were mentioned at least in 2 of the 4 publications are shown in Figure 3. Domains representing Health Related Quality of Life in LN patients are shown in Figure 3.



In the 3 studies analyzed including patients with Kidney Graft Failure, the experiences before, during and after the transplant failure and the impact on the caregiver burden were analyzed. Domains mentioned at least in 2 of the 3 publications are shown in Figure 4.



II. Gap analysis in AMR, DGF, LN and MN to measure Quality of Life

List of MN concepts considered for the gap analysis:

- Edema** and its impacts on **mobility, sleep quality, fatigue, pain, dressing difficulties**.
- Frequent urination** because of diuretic treatments and its impacts on sleep.
- Blood pressure fluctuations** (up and down very quickly);
- Social/family life impacts**.

List of COA considered for the gap analysis:

- EuroQoL 5-Dimension 5-Level (EQ-5D-5L)
- Kidney Disease Quality of Life instrument™ - 36 items (KDQOL-36™ Survey)
- Hospital Anxiety and Depression Scale (HADS)
- Patient-Reported Outcomes Measurement Information System - 29 (PROMIS-29)
- End-Stage Renal Disease Symptom Checklist- Transplantation Module (ESRD-SCL-TM)
- Ferrans and Powers Quality of Life Index - Dialysis version (QLI-Dialysis)
- Functional Assessment of Chronic Illness Therapy - Fatigue Scale (FACIT-Fatigue scale)
- Lupus Patient-Reported Outcome tool (LupusPRO)
- Urinary Incontinence-Specific Quality of Life (I-QOL)

Gap analysis in AMR and DGF:

- No AMR/DGF-specific questionnaire found.
- Current solution is to use a combination of generic PRO (e.g., **PROMIS-29**), and:
 - Administer a transplantation specific PRO (e.g., **ESRD-SCL-TM**); or
 - Develop **specific items to AMR/DGF** (e.g., transplantation failure / grieving for the loss/failure of transplant and the fear of going back to dialysis); or
 - For DGF patients only: use the **QLI-Dialysis**.

Alternatively, administer the **KDQOL-SF™** in addition to the **FACIT-Fatigue scale** and **AMR/DGF specific items**. Getting granularity around fatigue is more important than anxiety/depression, if a choice must be made.

Gap analysis in LN:

- Lupus-specific questionnaire available: **LupusPRO**.
- The **FACIT-Fatigue scale** is complementary to show a decrease in fatigue.

Gap analysis in MN:

- No MN-specific questionnaire found.
- Current solution is to use a combination of the following PROs:
 - an **Urinary questionnaire** (NOT on incontinence) + an **Edema questionnaire**; or
 - I-QOL** + an **Edema questionnaire**.

Notes: *The combinations of PROs don’t mean that the questionnaires must be administered at the same time, they can be administered at different time points. Sponsors should also balance the pros and cons of operational aspects (licensing, language, etc.).*

Additional aspects to consider:

- Use the EQ-5D-5L for utility values.
- Measure satisfaction with treatment (e.g., Renal Treatment Satisfaction Questionnaire).
- Minimise patient burden (number and lengths of PROs) to optimise data quality.
- Collect PRO data ideally prior to intervention/clinician interaction to minimise bias in responses.
- Conduct of in-trial interviews as a complement to evidence generation (e.g., mixed method), to test content validity of the PROs and to explore meaningfulness of change of PROs.