Quality of life in patients with Niemann-Pick disease type C and their carers

Jackson Pountney- Health Psychology
PhD student at Aston University

BACKGROUND

Niemann-Pick Disease (NPC):

• NPC is a very rare lysosomal storage disorder which has an incidence rate of around 1 in 100,000 people[1]
• Symptoms of NPC vary from person to person but can include: ataxia, vertical supranuclear gaze palsy, loss of motor function, psychiatric symptoms (psychosis, anxiety, depression, etc), respiratory dysfunction, hearing difficulties and many others [2,3]
• Clinical presentation and disease progression of NPC also vary greatly between a fatal condition presenting before birth (or early infancy) and a chronic neurodegenerative condition with onset occurring in adulthood [4]
• However there are no curative treatments available for NPC; only Miglustat which can offer some improvement in neurological symptoms [5]
• The life-limiting and degenerative nature of NPC can negatively impact the quality of life (QoL) of both persons living with NPC and those that care for them [1]

Quality of life (QoL):

• QoL is one of the most important outcome variables in rare disease research
• Improving QoL is often the highest priority in rare diseases where the disease course is chronic and there are no curative treatment options, such as NPC [6]
• QoL is commonly measured using patient-reported QoL questionnaires (or QoL scales)
• However, general QoL questionnaires may not be sensitive to the impact a specific disease has on patients' QoL, especially in NPC, where prognosis and symptom experience can vary so highly [6]
• Therefore, a QoL questionnaire specific to NPC is needed to accurately portray the elements of QoL that are mostimportant to patients

The Niemann-Pick disease type C Quality of Life Questionnaire (NPCQLQ):

• In 2019, the NPCQLQ was developed by Lydia Aston, Dr Rachel Shaw and Dr Rebecca Knibb at Aston University [7]
• Both adult and child versions of the NPCQLQ were developed
• However, these questionnaires have not yet been fully validated for wider use in the NPC population
• This means the questionnaires must first undergo rigorous statistical testing before they can be deemed valid,i.e. capable of truly measuring QoL in NPC patients, this is called scale evaluation
• The endpoint of scale evaluation is ensuring questionnaires are reliable (able to generate consistent results) and valid (accurately measures the concept they claim to measure) in being able to assess QoL [8]

Courtesy of: https://ec.europa.eu /eurostat/web/quality-of-life/data
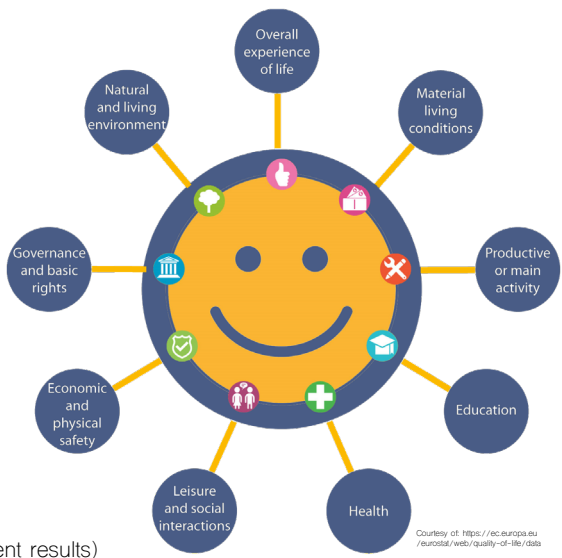
CURRENT PHD PROJECT

Funded by Aston University, Niemann-Pick UK (NPUK), the International Niemann-Pick Disease Registry (INPDR) and the National Niemann-Pick Disease Foundation (NNPDF):

• Builds on the previous work on the NPCQLQ
• Supervised by Dr Rebecca Knibb and Dr Gemma Mansell, based at Aston University
• The aims of the PhD are: to fully validate the NPCQLQ for use in both adult and child NPC patients, then use these questionnaires to identify outcome variables that may impact on QoL in NPC patients
• We are also planning to run additional studies which will widen the scope of this PhD – more on this in due course!

PHD OBJECTIVES

There are 4 main research objectives to be achieved across the 3 years of the PhD:

1) Fully validating both the adult and child versions of the NPCQLQ- Year one:
This will involve administering the questionnaires to NPC patients (or parent/carer proxies). The patient-reported data generated will be used to run statistical tests to assess the reliability (consistency) and validity (accuracy) of the NPCQLQ.It is hoped that there will be sufficient data for more sophisticated statistical tests, resulting in a robust QoL questionnaire for NPC patients.
2) Creating and validating shorter versions of the NPCQLQ- Year two:
Developing short forms of the NPCQLQ tools will enable rapid QoL assessment within clinical consultations and will also be less time-consuming for respondents to complete. Once these shorter forms of the NPCQLQ have been developed, they will be piloted with NPC patients, their carers and clinicians to determine their acceptability for wider use.
3) Exploring the impact of NPC on patient and carer QoL cross-sectionally- Year two
Here, we will look at NPC patient QoL cross-sectionally (at one time point) by analysing data the NPCQLQ in relation to other variables such as: disease severity, met/unmet needs, medication usage, clinical trial participation, economic/family impact and health service usage. This will provide insight into which aspects of living with NPC impact most on patients' QoL. We will then do the same for carer QoL and NPC patients across different counties, should we have sufficient data.
4) Exploring how NPC affects the QoL of both patients and their carers longitudinally– year three process from objective 3 will be carried out across multiple time points to assess patients'/carers' QoL longitudinally (over several points in time). It is likely that circumstances for NPC patients such as medication or symptom severity will change over time. The work in this objective will allow us to see whether the NPCQLQ can respond to changes in patients' circumstances over time. Again, this can be done for carer QoL and NPC patients across different counties if enough data is present.

WHAT THE PROJECT INVOLVES

• To achieve our objectives, we will analyse patient-reported data collected by the International Niemann-PickDisease Registry (INPDR)

• Patient involvement in this stage of the research is crucial!

• NPC patients and/or their carers will be asked to complete questionnaires on the INPDR patient-reported database

• Data from questionnaires concerning a variety of outcome variables will be used

• These include: patient QoL (general QoL and NPCQLQ), carer QoL, unmet needs, NPC disease/symptom severity, health service usage and more

• The NPCQLQ will undergo scale evaluation using patient-reported data from the INDPR

• The reliability (consistency) and validity (accuracy) of the NPCQLQ will be tested using this patient-reported data

• Once the NPCQLQ has been validated, the patient-reported data will be used to identify other variables which have the most impact on the QoL of NPC patients, in both the short term and across time

• We can also repeat this process to look at carer QoL and QoL of NPC patients across different countries if we have enough data

BENEFITS TO NPC PATIENTS & THE COMMUNITY

• A fully validated NPCQLQ will contribute significantly towards providing patients and their carers with a much needed voice in expressing how Niemann-Pick disease affects their lives
• When validated, the NPCQLQ can be included as an endpoint in clinical trials – will be able to tell if potential; new treatment results in meaningful changes to QoL experience of patients, i.e. beyond the improvement of symptoms
• This has implications for health technology assessment and drug reimbursement, drugs are more likely to be reimbursed if they are shown to improve QoL of NPC patients

REFERENCES

1. Bremova-Ertl, T., Claassen, J., Foltan, T., Gascon-Bayarri, J., Gissen, P., Hahn, A., ... & Schneider, S. A. (2021). Efficacy and safety of Nacetyl-l-leucine in Niemann–Pick disease type C. Journal of neurology, 1–12. DOI: 10.1007/s00415-021-10717-0
2. Mengel, E., Patterson, M. C., Chladek, M., Guldberg, C., Symonds, T., Lloyd-Price, L., ... & Burbridge, C. (2021). Impacts and Burden of Niemann Pick Type-C: A Patient and Caregiver Perspective. Orphanet J Rare Dis, 16(493), 1–14. DOI: 10.1186/s13023-021-02105-8
3. Rangel, D. M., Melo, M. C. A., Pedroso, J. L., Barsottini, O. G. P., Sobreira-Neto, M. A., & Braga-Neto, P. (2020). Beyond the Typical Syndrome: Understanding Non-motor Features in Niemann-Pick Type C Disease. The Cerebellum, 19(5), 722–738. DOI: 10.1007/s12311-020-01156-0
4. Geberhiwot, T., Moro, A., Dardis, A., Ramaswami, U., Sirrs, S., Marfa, M. P., ... & Patterson, M. (2018). Consensus clinical management guidelines for Niemann–Pick disease type C. Orphanet journal of rare diseases, 13(1), 1–19. DOI: 10.1186/s13023-018-0785-7
5. Maresca, G., Formica, C., Nocito, V., Latella, D., Leonardi, S., De Cola, M. C., ... & Corallo, F. (2021). Neuropsychological assessment in Niemann-Pick disease type C: a systematic review. Neurological Sciences, 1–9. DOI: 10.1007/s10072-021-05337-5
6. Lenderking, W. R., Anatchkova, M., Pokrzywinski, R., Skalicky, A., Martin, M. L., & Gelhorn, H. (2021). Measuring health-related quality oflife in patients with rare disease. Journal of Patient-Reported Outcomes, 5(1), 1–7. DOI: 10.1186/s41687-021-00336-8
7. Aston, L., Shaw, R., & Knibb, R. (2019). Preliminary development of proxy-rated quality-of-life scales for children and adults with NiemannPick type C. Quality of Life Research, 28(11), 3083–3092. DOI: 10.1007/s11136-019-02234-5
8. Boateng, G. O., Neilands, T. B., Frongillo, E. A., Melgar-Quiñonez, H. R., & Young, S. L. (2018). Best practices for developing and validating scales for health, social, and behavioral research: a primer. Frontiers in public health, 6(149), 1–18. DOI: 10.3389/fpubh.2018.00149

Jackson Pountney
PhD student at Aston University
Email: 200216137@aston.ac.uk