DETERMINING TREATMENT PREFERENCE FOR TOLVAPTAN IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): DEVELOPMENT OF A DISCRETE CHOICE EXPERIMENT FOR USE AS A CLINICAL STUDY ENDPOINT

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Introduction

- ADPKD is a rare, hereditary, progressive condition characterised by the development of renal cysts, leading to decreased quality of life and ultimately, for most patients, kidney failure[1,2]. Tolvaptan (Jinarc®) is licensed in Europe to slow the progression of ADPKD in patients initiating treatment in CKD stages 1-3 with evidence of rapidly progressing disease
- A known and expected adverse effect of tolvaptan is aquaresis; there is sparse evidence on the impact of tolvaptan-related aquaresis on patient health-related quality of life (HRQoL)[3]
- Discrete Choice Experiments (DCEs) elicit patient preference for attributes of healthcare interventions
- ACQUIRE is a prospective, real-world, non-interventional study that aims to describe the impact of tolvaptan on HRQoL and other patient reported outcomes. ACQUIRE will include a DCE aiming formally to quantify the relative strength of preference of patients for the likely positive and negative attributes of tolvaptan

Objectives

- To develop a DCE quantifying patient preference for disease modifying treatment over symptom control alone
- To assess the feasibility of a DCE as an exploratory endpoint in a prospective non-interventional study

Methods

- 20 patient and 8 physician concept elicitation interviews were conducted to derive a conceptual model for ADPKD to which the DCE could be mapped (**Figure 1**)
- A DCE instrument was constructed based on five key attributes predicted to be impacted by the initiation of tolvaptan. Each attribute is associated with three levels (**Table 1**)
- Patients will choose their preferred option across a series of hypothetical 'pairwise' treatment options (**Figure 2**)
- Validation steps included cognitive debriefing interviews and a pilot of the DCE instrument itself in a small number of patients (n=5)

Figure 2. Example of Pairwise Choice Set

Which treatment for ADPKD would you choose in addition to your other medications for symptoms (such as high blood pressure, if these were your only two options?

Choice 1	Treatment A	Treatment B
Time to kidney failure (ESRD)	Delay of 5 years to kidney failure	Delay of 2.5 years to kidney failure
Risk of serious and permanent liver damage	No increase of serious and permanent liver damage	2.5 in 10,000 increased risk of serious and permanent liver damage
Additional doctor/clinic visits	No more visits	1 more visit per month for 18 months, then one more visit every 3 months
Increased urinary frequency and excessive thirst	No additional urination or increased thirst	You go to the toilet and have to drink twice as much
Tablet number and routine	One more tablet in the morning	2 more tablets per day morning and evening

Which treatment do you prefer? (Please select one box)

Treatment A ☐   Treatment B ☐

Would you be willing to take this treatment?

Yes ☐   No ☐

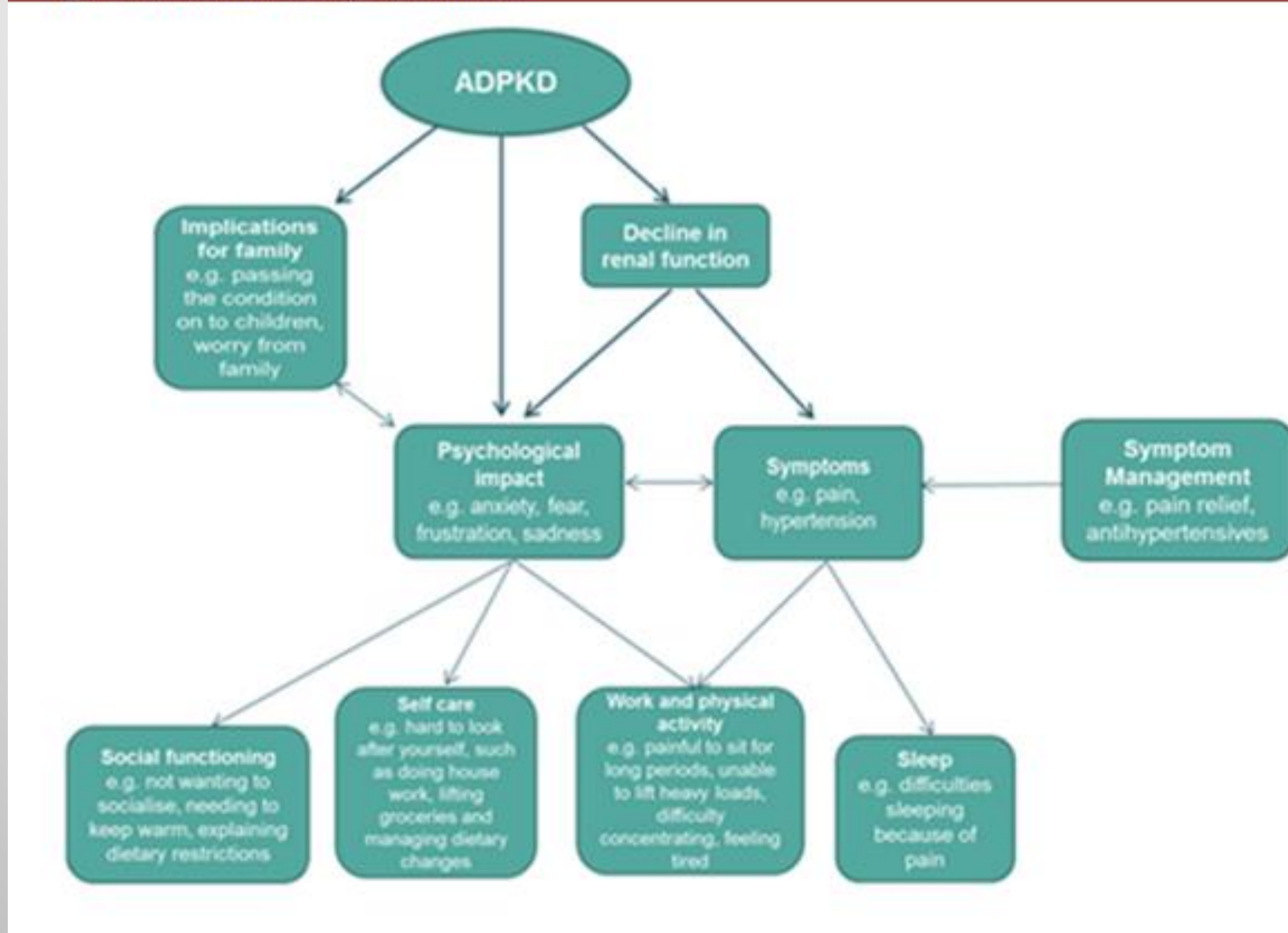### Figure 1. ADPKD Conceptual Model

Conclusion/Discussion

- The use of DCE as an exploratory study endpoint has potential to complement overall study objectives
- This pilot indicates that patients may be willing to accept the main drawback of tolvaptan in exchange for gaining time to kidney failure, and warrants further investigation/validation
- The DCE methodology outlined in this poster has demonstrated internal and external consistency and will be included in the ACQUIRE study as an exploratory endpoint

Results

- Cognitive debriefing validated the attributes and levels
- Time to kidney failure dominated other attributes including aquaresis in terms of driving patient choice
- In 91% of all choice sets, patients preferred the treatment with the longer time to kidney failure
- In all choice sets, at least 60% of patients said they would like to take their preferred treatment
- As such, pilot results indicate that the hypothesis of patients tolerating/adapting to negative effects such as aquaresis in exchange for an increase in time to kidney failure, warrants further investigation

Table 1. DCE Attributes and their associated levels

Time to kidney failure	Delay of 6 months to kidney failure	Delay of 2.5 years to kidney failure	Delay of 5 years to kidney failure
Risk of liver damage	No increased risk of serious and permanent liver damage	2.5 in 10,000 increased risk of serious and permanent liver damage	5 in 10,000 increased risk of serious and permanent liver damage
Additional doctor/clinic visits	No more visits	1 more visit per month for 18 months, then 1 more visit every 3 months	2 more visits per month for 6 months, then 1 more visit every month
Increased urinary frequency and excessive thirst (Aquaresis)	No additional urination or increased thirst	You go to the toilet and have to drink twice as much	You go to the toilet and have to drink three times as much
Number of tablets and routine to follow	One more tablet in the morning	2 more tablets per day, morning and evening	2 more tablets per day taken exactly 8 hours apart

References: 1. Torres VE, Harris PC, Pirson Y: Autosomal dominant polycystic kidney disease. Lancet 369: 1287–1301, 2007. 2. Grantham JJ: Clinical practice. Autosomal dominant polycystic kidney disease. N Engl J Med 359: 1477–1485, 2008;. 3. Torres VE, Chapman AB, Devuyst O, et al. Tolvaptan in patients with autosomal dominant polycystic kidney disease. The New England journal of medicine. Dec 20 2012;367(25):2407-2418.

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