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# ADAPTING THE ADPKD OUTCOMES MODEL TO PREDICT COST CONSEQUENCE IN ITALIAN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD) TREATED WITH TOLVAPTAN

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## BACKGROUND

ADPKD (Autosomal Dominant Polycystic Kidney Disease) is a severe genetic disorder with an estimated prevalence less than 4 patients per 10.000 inhabitants in EU. (1). ADPKD is characterised by the formation of renal cysts, which progressively compress normal tissue with loss of renal function and damage to adjacent tissues [2, 3]. With progression of the disease patients reach the terminal stage (ESRD) of chronic kidney disease. [4]

There is currently no overall consensus regarding prediction of the rate of progression in ADPKD, especially in the early stage of disease largely due to the high degree of inter-patient variability. [5]

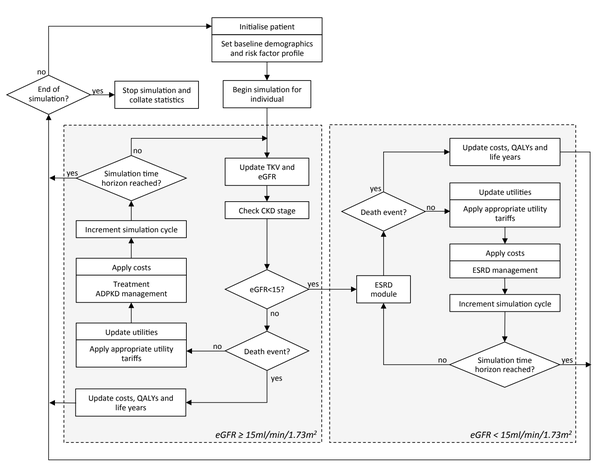
## OBJECTIVES

This study aimed to adapt the ADPKD Outcomes Model [5,6] in order to compare the progression to ESRD and relative costs of disease, comparing patients treated with the tolvaptan as to non-treated patients in Italy.

## METHODS

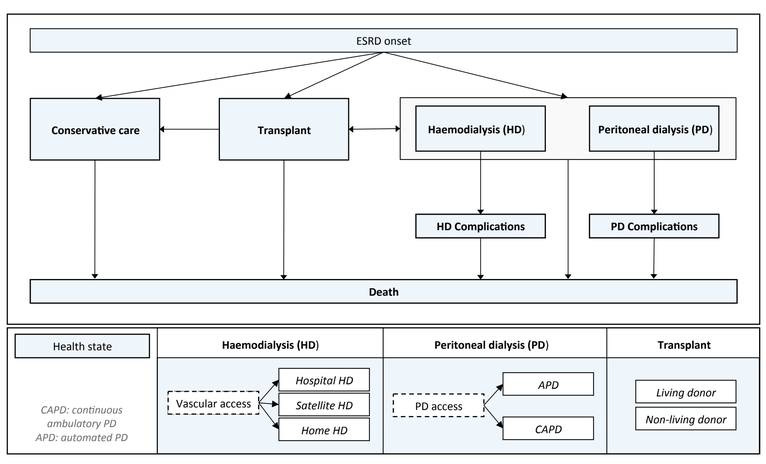
Utilising the structure of the ADPKD Outcomes Model *(Figure 1)* adapted to the Italian context, the analysis has simulated the evolution of ADPKD patients over a period of up to 80 years. The study was performed from both the Italian National Health Service (NHS) and social perspectives. The ADPKD Outcomes Model is based on a series of annual simulations at the individual patient level that allows clinical evolutions, such as the achievement of end-stage renal disease (ESRD) *(Figure 1)*.

***Figure 1. ADPKD Outcomes Model schematic***




The model is able to incorporate country-specific pathways for ESRD-affected patients, such as haemodialysis (HD), peritoneal dialysis (PD), transplant and conservative therapy (RRT), together with their different costs and mortality rates *(Figure 2)*. Clinical data on the treatment effect of tolvaptan was derived from the TEMPO 3:4 clinical trial [7].

***Figure 2. ESRD[1] module schematic***




[1] End Renal Stage Disease

## RESULTS

The results show that tolvaptan is estimated to postpone the time to ESRD by a mean of around 3.7 years and increase life expectancy by a mean of 1.6 years. It is predicted that a large number of ESRD events and deaths could be avoided among patients treated with tolvaptan vs non-treated patients (346 ESRD events avoided and 68 deaths due to ESRD avoided at 15 years) *(Figure 3)*.

***Figure 3. Cumulative difference for ESRD events, ESRD death and death for other causes***




It was also estimated *(Figure 4)* that, at 15 years, treatment with tolvaptan is estimated to increase the number of patients remaining in CKD stages 1-4 and reduce the number of patients in ESRD (i.e. 1070 patients non-treated in ESRD vs 361 patients treated with tolvaptan in ESRD at 15th year). Correspondingly, it was estimated that treatment with tolvaptan reduces the number of patients who need transplant, haemodialysis (HD), peritoneal dialysis (PD) or conservative care *(Figure 5)*.

***Figure 4. Number of living patients by CKD[2] stage***

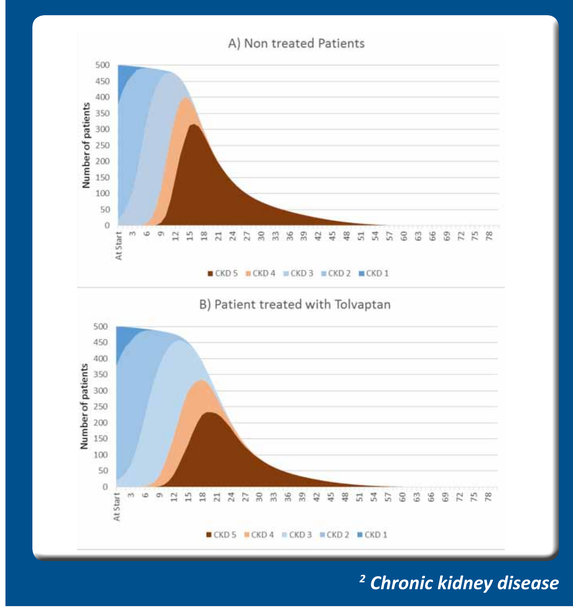
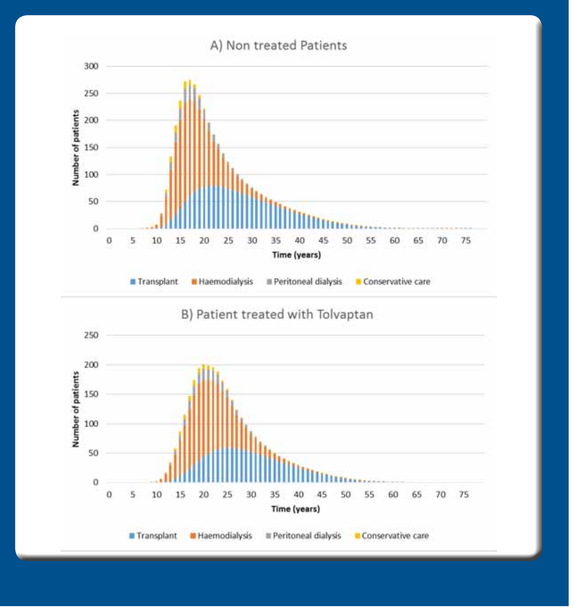



***Figure 5. Distribution of patients across ESRD treatment modalities***




[2] Chronic kidney disease

Moreover, patients treated with tolvaptan are estimated to be associated with a considerable reduction in direct and indirect health costs (at 15 years, €17.600.882 saved for direct cost and €5.829.239 saved for indirect cost). Accordingly, the cumulative cost per patient treated with tolvaptan is estimated to be lower than of non-treated patient, with an average difference per patient of €36.426, of which €27.133 for direct costs and €9.294 for indirect costs. *(Figure 6)*

Breaking down the direct cost savings, Figure 7 shows these are distributed among the treatments of ESRD: at 15 years the cumulative difference between the two arm of treatments is equal to € 16.622.166 for HD, € 2.004.383 for PD, € 2.723.423 for transplant, € 582.134 for conservative care.

***Figure 6. Cumulative direct and indirect costs***

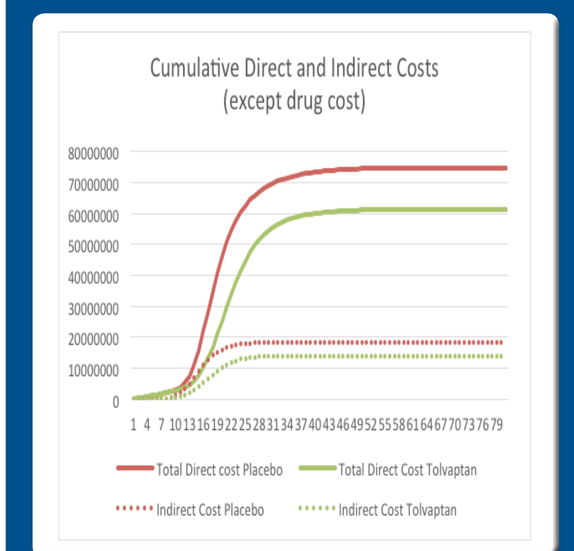
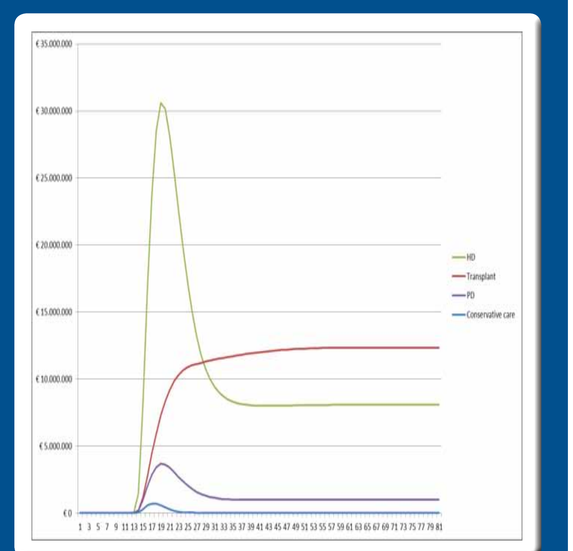



***Figure 7. Cumulative difference for HD , PD , transplant and conservative care costs***




## CONCLUSIONS

The use of tolvaptan in patients with ADPKD is estimated to permit a slowing down in the worsening of the disease, increasing life expectancy and the achievement of a considerable decrease in the direct and indirect health costs in the medium to long-term

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