COMPARISON OF THE COST-EFFECTIVENESS OF THE URINARY BASED CKD273 BIOMARKER PANEL AND CURRENT CLINICAL PRACTICES IN THE MANAGEMENT OF CHRONIC KIDNEY DISEASE PROGRESSION

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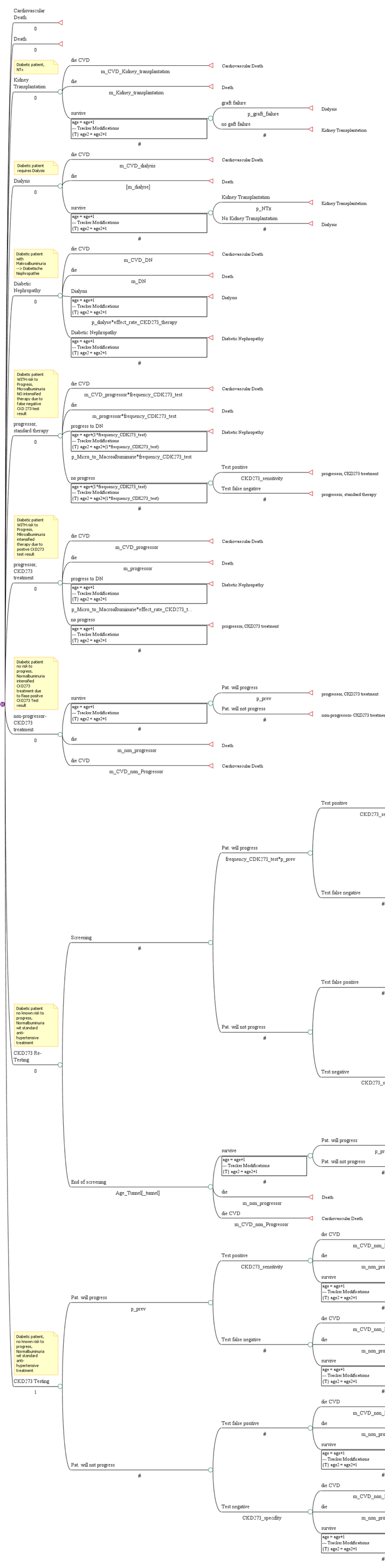
Fig.1: Markov Node for CKD273, including diabetic complications and/or patient-oriented outcomes.
(Due to space limitations we will not provide the analoge node for UAE)



INTRODUCTION

Diabetic nephropathy is the leading cause of chronic kidney disease (CKD) in patients initiating renal replacement therapy. To date, urinary albumin excretion (UAE) and/or sustained decline in estimated glomerular filtration rate are applied to identify patients at highest risk for developing CKD progression. Recently a multidimensional urinary based biomarker panel, namely CKD273, was developed based on Capillary Electrophoresis – Mass Spectrometry techniques. This non-invasive biomarker panel has demonstrated superior accuracy than the current clinical standard of urinary albumin excretion (UAE) in detecting and predicting CKD progression [Siwy et al. NDT 2014;29:1563-70]. The study aim was to compare the cost-effectiveness of the CKD273 panel, as opposed to the current clinical standard of UAE, for predicting CKD progression and deterring associated adverse outcomes within German clinical settings.

Methods

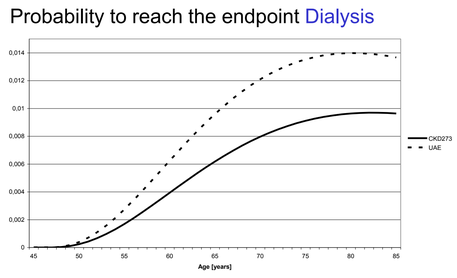
The TreeAge Pro software programme (USA) was utilized to develop a Markov model, including annual cycles from the age of 45 to 85 years or death. The model included an inception cohort of diabetic patients, free of CKD symptoms and/or other disease related complications, and at risk of developing one or more of the following diabetic complications and/or patient-oriented outcomes: microalbuminuria, macroalbuminuria/diabetic nephropathy, renal dialysis, renal transplantation, and/or death (differentiated between death attributable to cardiovascular diseases and death from all other causes) (Fig.1). Both the probabilities of these events and incurred healthcare associated costs are primarily based on data from Germany, or otherwise on the UKPDS 64 study. In the event of a positive biomarker panel result, it was assumed that patients would be administered intensified therapeutic schemes and thus experience delayed disease progression.

Results

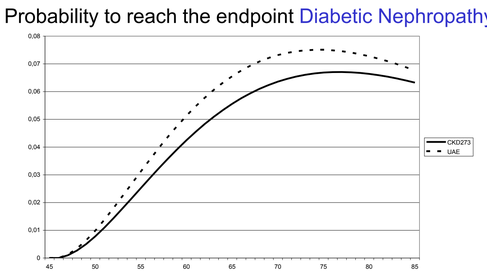
The CKD273 biomarker panel (sensitivity 94.6%, specificity 97.1%) displayed greater cost- efficiency than the current clinical standard of UAE testing (sensitivity 96.7%, specificity 71.0%). Upon the conclusion of the study period, the overall cost per patient was 17,567.00 € lower in the CKD273 biomarker panel group as compared to the UAE group. In addition, the frequency of patients requiring renal dialysis was reduced by 30% in the CKD273 biomarker panel group, as compared to the UAE group (Fig.2). Finally, approximately 10,000 cardiovascular deaths, as well as an additional 5,000 deaths from all other causes, were projected to be deterred in the CKD273 biomarker panel group (Table 1).

Fig.2: Probabilities to reach the different Endpoints Dialysis, Diabetic Nephropathy or Kidney Transplantation for both study groups.

Probability to reach the endpoint Dialysis



Probability to reach the endpoint Diabetic Nephropathy



Probability to reach the endpoint Kidney Transplantation

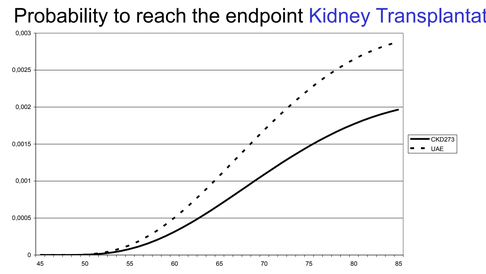


Table 1: Number of estimated death (differentiated between death attributable to cardiovascular diseases and death from all other causes) in the CKD273 biomarker panel group, as compared to the UAE group

	CKD273			UAE			Diff UAE - CKD		
Years	Cardiovascular Death	Death	Total	Cardiovascular Death	Death	Total	Cardiovascular Death	Death	Total
5	39.956	35.343	75.299	39.999	35.351	75.350	43	7	51
10	89.243	70.678	159.920	89.765	70.833	160.598	522	155	678
15	143.652	105.011	248.663	145.370	105.627	250.998	1.719	616	2.335
20	199.804	137.638	337.442	203.297	139.026	342.323	3.493	1.389	4.881
25	255.054	168.016	423.070	260.565	170.370	430.935	5.511	2.354	7.865
30	307.486	195.776	503.262	314.926	199.138	514.064	7.440	3.362	10.802
35	355.855	220.718	576.573	364.892	225.006	589.898	9.037	4.288	13.325
40	399.470	242.791	642.261	409.643	247.841	657.484	10.173	5.050	15.223

Conclusions:

The urinary based CKD273 biomarker panel outperforms the current clinical standard of UAE testing with respect to both accuracy and cost-efficiency for detecting CKD progression. Notable diminution of adverse patient outcomes and healthcare associated costs could be achieved through the adoption of the CKD273 panel within German healthcare settings. The potential utility of the CKD273 panel for optimally deterring CKD progression whilst reducing healthcare costs ought to be confirmed in other European settings

Table 2: Variables used in the model

Name	Description	Source	Value
age	Age of Patients		start_age
start_age	age of patients at beginning of modelling		45
CKD273_specifity	Specificity of CKD273 to detect Markoalbuminuria/ Diabetic Nephropathy	Rossing et al Diabetologica 2010 53(Supplement 1) S480-S481	0.971
CKD273_sensitivity	Sensitivity of CKD273 to detect Markoalbuminuria/ Diabetic Nephropathy	Molin et al Journal of Proteomics 2012 75:5888-5897	0.946
UAE_Specificity	Specificity of Urinary albumin excretion testing to detect Markoalbuminuria/ Diabetic Nephropathy	Morgensen et al Diabetes Care 1997 20:1642-1646	0.710
UAE_sensitivity	Sensitivity of Urinary albumin excretion testing to detect Markoalbuminuria/ Diabetic Nephropathy	Morgensen et al Diabetes Care 1997 20:1642-1646	0.967
m_non_progressor	mortality non-progressor (Normoalbuminurie) without CV Death	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.007
m_progressor	mortality progressors (Microalbuminuria) without CV Death	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.01
m_DN	mortality Diabetic nephropathy (Markoalbuminuria) without CV Death	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.011
m_dialyse	mortality dialysis without CV Death	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.071
m_kidney_transplantation	mortality after kidney transplantation without CV Death	Boucek et al NDT 2002;17:1678-1683	0.043
m_CVD_non_Progressor	cardiovascular mortality non-progressor (Normalbuminurie)	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.007
m_CVD_progressor	cardiovascular mortality progressors (Microalbuminuria)	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.02
m_CVD_DN	cardiovascular mortality Diabetic Nephropathy (Macroalbuminuria)	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.035
m_CVD_dialysis	cardiovascular mortality dialysis	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.121
m_CVD_Kidney_transplantation	cardiovascular mortality kidney transplantation	Boucek et al NDT 2002;17:1678-1683	0.019
frequency_CDK273_test	annual test frequency of CKD273 Test (1= every year;2 = each 2 years)		1
frequency_UEA	annual test frequency of UAE Test (1= every year;2 = each 2 years)		1
effect_rate_CKD273_therapy	effect of CKD273 therapy		0.68
effect_rate_UAE	effect of UAE therapy	Farmer et al Health Technol Assess 2014; 18(14)	0.88
c_CKD273	annual Costs for CKD273 Testing		966.11 €
c_UAE_Test	annual Costs for UAE Testing		36.16 €
c_dialysis	annual costs for a dialysis Patient	http://www.kasseler-symposium.de/documents/Rueckblick/Plum_AOK_Gesundheitspolitische_Aspekte.pdf	52,968 €
c_Diabetic_Nephropathy	annual Costs for a patient with diabetic nephropathy	Bierwirth et al Der Diabetologe 2008; 4:549-555 – Mean costs	5,987 €
c_Kidney_transplantation	medication cost with funtional graft	http://www.transplantation.de/fileadmin/transplantation/txmedizin/txmedizin_2007_3/04_lattrell.pdf– Mean costs	13,000 €
c_graft_rejection	cost for graft rejection		70,000 €
c_NTx_grafting	Cost for a kidney transplantation	DRG 2012 – Mean A17 A+B	21,896.50 €
c_modified_therapy	annual Costs modiefied therapy w/o standard therapy	Manns et al BMJ 2010; 341:c5869 (additional ACE/AT1 inhibitor)	378.00 €
c_standard_therapy	annual costs standard therapy	Manns et al BMJ 2010; 341:c5869 (Medication for people with known CKD per year without ACE/AT1 inhibitor)	857.00 €
c_CKD273_therapy	annual coasts CKD273 therapy minus standard therapy		420.00 €
c_cardiovascular_death	Costs cardiovascular death	Statistisches Bundesamt Costs/Number od Death by CV Disease (ICD10 I00 - I99)	103,644.50 €
QALY_NTx	disutility QUALY factor NTx		0.76
QALY_Dialyse	disutility QUALY factor dialyse		0.48
QALY_noESRD	disutility QUALY factor no ESRD		0.88
p_dialyse	annual rate of transition from Diabetic Nephropathy to Dialysis		0.0453
p_Normo_to_Microalbuminurie	annual rate of transition from Normo to Microalbuminuria	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.0200
p_Micro_to_Macroalbuminurie	annual rate of transition from Micro to Makroalbuminurie	UKPDS 64 study (Adler et al. Kidney Int 203; 63:252-263)	0.0280
p_NTx	annual rate of transplanted kidneys	DSO Jahresbericht 2012 2586 kidney transplantations / 82823 dialysis patients	0.0312
p_graft_failure	annual rate of graft lost	DSO Jahresbericht 2012 overall 5 years graft survival 74,3% in Germany	0.0514

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