1. Scientific background

The **DiaPat-CoV-50** test is based on the analysis of 50 defined urine peptides whose presence in the urine is statistically significantly associated with a critical course (WHO grade 6 or higher) of a SARS-CoV-2 infection.

As part of the study, urine samples were collected from patients suffering from Covid-19. Three time points were defined: time point 1: 0-1 day after the infection was detected (positive test result for SARS-CoV-2); time point 2: 4-7 days after the infection was detected; time point 3: 10-21 days after detection of the infection.

The urine samples were analyzed with the capillary electrophoresis coupled mass spectrometry (CE-MS) approach, which is already used for the diagnosis of several other diseases.

The **DiaPat-CoV-50** test, based on urinary peptides significantly associated with a severe course of Covid-19, was used prospectively on all patient samples from time point 1. The prediction of death and worsening of the disease (defined by WHO scores) was tested. The association of the **DiaPat-CoV-50** value with the highest WHO score achieved during the follow-up was also determined.

2. Description of the "DiaPat-CoV-50" including calculation basis for the test

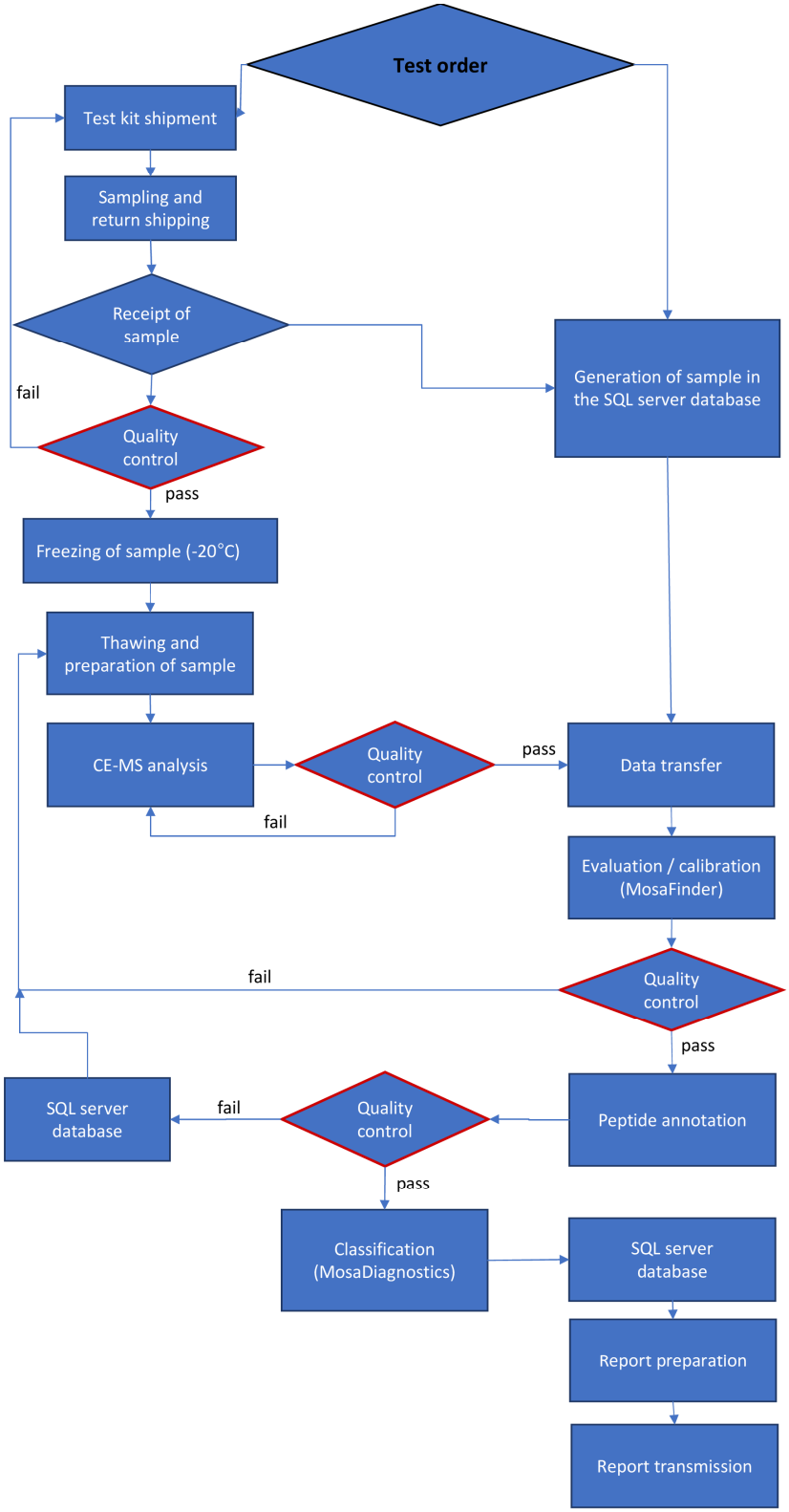

Figure 1. *Graphic depiction of CE-MS analysis and subsequent data evaluation*

The entire analytical process from shipment to report transmission is graphically depicted in **Figure 1**. The methods used and the results of the investigations are given below.

2.1. METHODS

2.1.1. Sample preparation

A 0.7-mL aliquot of urine is diluted with 0.7 mL of an aqueous solution supplemented with 2 M urea, 10 mM NH4OH, and 0.02 % sodium docecyl sulfate. To remove proteins of higher molecular weight, the sample is filtered using Centrisart ultracentrifugation filter devices (20 kDa molecular weight cut-off; Sartorius, Goettingen, Germany) at 3,000 rcf for 45 min at 4 °C. Subsequently, 1.1 ml of filtrate is applied onto a PD-10 desalting column (GE Healthcare, Germany) equilibrated in 0.01% NH4OH in HPLC-grade water to remove urea, electrolytes, and salts. Finally, all samples are lyophilized and resuspended in HPLC-grade water shortly before analysis. (Theodorescu et al., 2006).

2.1.2. CE-MS analysis

All urine samples are prepared using a standard protocol and are analyzed by capillary electrophoresis coupled to mass spectrometry (CE-MS). CE-MS analysis is performed with a P/ACE MDQ capillary electrophoresis system (Beckman Coulter, USA) coupled to a micro-TOF-MS (Bruker Daltonic, Germany). The electro-ionization sprayer (Agilent Technologies, USA) is grounded, and the ion-spray interface potential is set between -4.0 and -4.5 kV. MS data acquisition and acquisition of experimental parameters are automatically controlled by the CE via contact closure. Spectra are accumulated every 3 seconds, over a range of m/z 350 to 3,000.

The analytical performance of the CE-MS system was examined and described in detail by Mischak et al. (Mischak et al., 2013). Based on individual peptides, the average recovery of the sample preparation was approx. 85%, with a detection limit of ~ 1 fmol (see also below under performance characteristics of the platform). Monoisotopic mass signals were resolved for $z \leq 6$. The mass accuracy of the CE-TOF-MS method was determined to be <25 ppm for monoisotopic resolution and <100 ppm for unresolved peaks ($z > 6$).

2.1.3. Mass spectrometric data processing and data calibration

Mass spectral ion peaks representing identical molecules at different charge states (m/z with z=1, 2, 3…) are deconvoluted into single masses using proprietary software MosaiquesFinder. Only signals were taken into account that were observed in at least 2 consecutive spectra with a signal-to-noise ratio of at least 4. Signals with a charge of +1 were excluded in order to minimize interference with low molecular weight substances. MosaiquesFinder employs a probabilistic clustering algorithm and uses both isotopic distributions as well as conjugated masses for charge-state determination of peptides/proteins. TOF-MS data were calibrated utilizing FT-ICR-MS data as reference masses applying linear regression. Both CE-migration time and ion signal intensity (amplitude) show variability, mostly due to different amounts of salt and peptides in the sample. To correct for this variability, a linear regression algorithm was applied with internal standard peptides as reference. Reference signals of over 3151 urinary peptides were used

for CE-time calibration by local regression The analysis of the peptide's abundance is semi-quantitatively performed in reference to internal standards (Jantos-Siwy et al., 2009; Theodorescu et al., 2006). We use 29 collagen fragments that are generally found in urine and that do not appear to be highly significantly associated with disease as internal standard, as described in detail in (Jantos-Siwy et al., 2009). The final result is a peak list, characterizing each protein and peptide by its molecular mass [Da] and normalized CE migration time [min]. Normalized signal intensity is used as a measure for relative abundance. The entire analytical process is also graphically depicted in **Figure 1**.

The use of an array of 29 internal standards results in higher stability, even if one of the internal standard peptides is identified as a potential biomarker. In the case an internal standard peptide is significantly altered in a urine sample (compared to the other internal standard peptides), the calibration algorithm takes this into account and the weighting for normalization of this peptide is lower that for the others. This phenomenon is shown in **Figure 2**, were regulated standard peptides are depicted in a pale dot, in contrast to the non-regulated standard peptides.

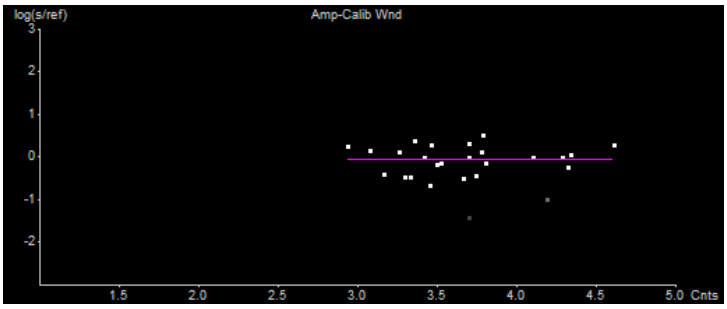

Figure 2: *Weighting of internal peptide standards. The x-axis shows the logarithmic amplitude (counts) of the measured peptides and the y-axis depicts the regulation factor (log(amplitude$_{sample}$/ampitude$_{reference}$)). Relevance (weighting) of the individual peptides is reflected by intensity.*

2.1.4. SVM classification model

A Support Vector Machine (SVM) performs classification by constructing an N-dimensional hyperplane that optimally separates subjects (e.g. case and controls) into two categories. A set of features that describes a subject i (i.e., a row builds by N intensities of the biomarkers) is called a vector and denoted here by xi. The coordinates of the vector xi used to define the hyperplane are called features. The task of choosing the most suitable features is known as feature selection, i.e. selection of case-specific markers.

The aim of SVM classification is to find the optimal hyperplane that separates clusters of vectors in such a way that case subjects are on one side of the plane and controls are on the other size of the plane. The vectors near the hyperplane are called support vectors. If the two classes are separable, the simplest way to distinguish either group would be a flat (N-1)-dimensional plane embedded in the N-dimensional space. In reality, the points in the

case/control study are separated by a nonlinear region. Instead of trying to fit nonlinear curves to the data, SVM handles this by using a kernel function to map the data into a different space, where a hyperplane can be found to do the separation. MosaCluster software uses Gaussian basis radial functions (RBF) for transforming the data into a higher dimensional space to make the separation possible. The RBF are defined as

$$K(x_i, x_j) = \Phi(x_i)\Phi(x_j) = \exp(-\gamma \| x_i - x_j \|^2)$$

with γ=1/(2²); γ>0 as kernel parameter and ⍰ as Gaussian mapping function in the feature space. Hence γ controls the width of SVM kernel. Support vector classification using a Gaussian RBF kernel is sensitive to the kernel width. Small kernel widths may cause over-fitting, large kernel widths under-fitting, respectively. The so-called optimal kernel width is merely selected based on the tradeoff between under-fitting loss and over-fitting loss. The kernel is indeed a way of taking advantage of the fact that separation may be easier in higher dimensions as schematically indicated in **Figure 3**.

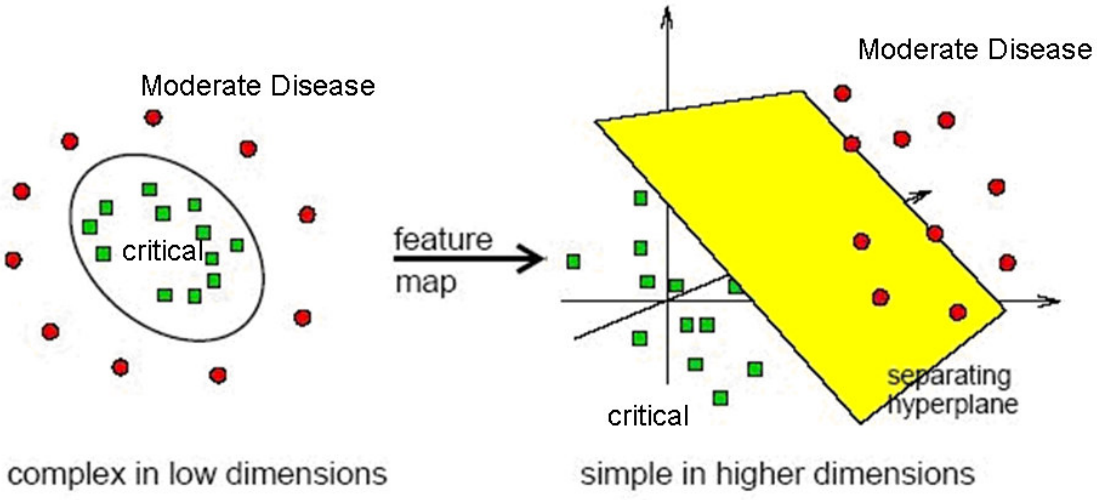

Figure 3: *Schematic illustration of the effect observed for transforming the original data to a higher dimensional feature space using kernels. In two dimensions a non-linear curve is necessary to separate CKD (green squares) from non-CKD patients (red dots). Mapping the data into a three-dimensional feature space allows for the separation of both groups with a simple 2-dimensional plane (yellow).*

Ideally SVM classification should produce a hyperplane that completely separates the subjects into two non-overlapping groups. However, in reality perfect separation is often impossible. To allow some misclassification and hence introducing some flexibility in separating case and control subjects, the SVM model has a so-called cost or penalty parameter C with C>0, that controls the tradeoff between allowing training errors and forcing rigid margins. It creates a soft margin that permits some misclassifications. Increasing the value of C increases the cost of misclassifying points and forces the algorithm to adapt the model to a higher extend to the training dataset. However, a highly adapted model may not generalize well in independent datasets, a phenomenon called over-fitting.

The accuracy of an SVM model is largely dependent on the selection of the model parameters C and γ. Therefore, these are optimized via cross-validation in the training set. For the **DiaPat-CoV-50** test, the following SVM parameters were determined in the training set (samples from time point 2 and 3, NO samples from time point 1) and then fixed:

Parameter specification:

SVM library: LIBSVM http://www.csie.ntu.edu.tw/~cjlin/libsvm
Kernel function: Gaussian basis radial function (RBF)
Kernel width γ: 0.00002
Cost or penalty parameter C: 1000
Number of features (biomarkers) N: 50
Dimensionality of separating hyperplane (N-1): 49

These parameters describe the exact classification algorithm. For the establishment of the model, as well as for the subsequent application, the normalized log-transformed amplitudes of all 50 peptides (listed in **Figure 4**) in a sample were used.

Pr_ID	mean Amp. Moderate	mean Amp. Critical	Sequence	Gene Symbol
99901583	19,24	1719,05	GGSKRISIGGGS	KRT6A
99902592	375,72	41,6	DDGEAGKpGRpG	COL1A1
99902858	947,4	200,95	EAGGGSNSLQNSP	FRMD4A
99904531	4326,09	789,54	PGTpGSPGPAGASGNPG	COL2A1
99904813	1868,59	989,06	FDVNDEKNWGLS	ORM1
99905288	474,14	190,85	FPGQTGPRGEMGQp	COL7A1
99905387	286,62	113,64	GLSMDGGGSPKGDVDP	FXYD2
99905551	3164,94	1090,06	VGPpGPPGPpGPpGPPS	COL1A1
99905677	5376,04	1698,97	pGKDGDTGPTGPQGPQ	COL22A1
99905682	9031,31	2178,81	VGPpGPpGPpGPpGPPS	COL1A1
99905830	3224,14	1275,1	GPpGVPGpPGpGGSPGLP	COL22A1
99906154	612,63	88,19	EDGHpGKPGRpGERG	COL1A2
99906182	606,21	115,65	GpAGPRGERGPpGESGA	COL1A2
99906213	291,15	28,04	NDGApGKNGERGGpGGp	COL3A1
99906516	1322,93	97,32	SGQSSGYTqhGSGSGh	HRNR
99907622	1797,07	486,91	WVGTGASEAEKTGAQEL	GSN
99909548	476,21	11,04	GTDGpMGpHGpAGPKGERGE	COL25A1
99910424	786,63	30,32	EEDDGEVTEDSDEDFIQP	TRIM33
99910554	8380,2	3390,06	EGSpGRDGSpGAKGDRGETGPA	COL1A1
99911193	1956,44	1026,63	NSGEpGApGSKGDTGAkGEpGPVG	COL1A1
99911382	6,97	118,28	AGPpGKAGEDGHPGKPGRpGERG	COL1A2
99911417	174,19	1826,72	KGEKGDSGASGREGFPGVpGGTGP	COL7A1
99911629	63,69	1994,02	AGPpGKAGEDGHpGKpGRpGERG	COL1A2
99911826	340,16	1707,77	SETAPAAPAAPAPAEKTPVKKKA	H1-4
99913428	197,67	4831,15	LmlEQNTKSPLFMGKVVNPTQK	SERPINA1
99914152	170,09	7,96	DDPRPPNPPKPMPNPNPNHPSSSGS	CD99
99914935	16,16	196,68	GPpGPKGNSGEpGApGSKGDTGAKGEpGPVG	COL1A1
99915129	730,34	224,72	ERGEAGIpGVpGAKGEDGKDGSPGEpGANG	COL3A1
99915360	923,07	282,81	GpKGDpGIpGLDRSGFpGETGSPGIPGHQ	COL4A3
99915400	317,25	1950,67	LkGQpGApGVkGEpGApGENGTpGQTGARG	COL1A2
99915411	3577,47	635,96	PQGPpGPTGpGGDKGDTGPpGPQGLQGLpGT	COL3A1
99915863	3424	1670,57	ESGREGApGAEGSpGRDGSpGAKGDRGETGP	COL1A1
99916966	1270,59	228,26	PpGESGREGApGAEGSpGRDGSPGAKGDRGETGP	COL1A1
99917047	6011,17	1369,08	PpGESGREGApGAEGSpGRDGSpGAKGDRGETGP	COL1A1
99917105	89,12	1040,32	TGAKGAAGLpGVAGApGLpGPRGIpGPVGAAGATGARG	COL1A2
99917754	1082,25	102,7	GFAGPPGADGQPGAKGEPGDAGAKGDAGPPGPAGPAGpPG	COL1A1
99917946	2401,09	1009,59	PpGPAGFAGPPGADGQPGAKGEpGDAGAKGDAGPPGPAGP	COL1A1
99917947	1557,41	384,23	GSEGPQGVRGEPGpPGPAGAAGPAGNPGADGQPGAKGANG	COL1A1
99918281	596,66	54,22	ppGSNGNpGPPGPPGPSGKDGPKGARGDSGPPGRAGEPG	COL2A1
99918378	471,74	21315,77	EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAE	SERPINA1
99918782	937,97	182,4	GRPEAQPPPLSSEHKEPVAGDAVPGPKDGSAPEVRGA	VGF
99918807	161,5	0	HVSGSGQSSGFGQHESRSGHSSYGQHGFGSSQSSGYG	FLG2
99918864	609,23	58,18	SGPPGRAGEPGLQGPAGPpGEKGEPGDDGpSGAEGPpGPQG	COL2A1
99918915	293,37	43,97	EEKAVADTRDQADGSRASVDSGSSEEQGGSSRALVST	PIGR
99919107	456,38	59,72	DQGPVGRTGEVGAVGPpGFAGEKGpSGEAGTAGPPGTpGPQG	COL1A2
99919635	1866,11	104,12	DADLADGVSGGEGKGGSDGGGSHRKEGEEADAPGVIPGIVGAVV	CD99
99919753	340,14	4131,07	GPEGPSGKpGINGKDGIPGAQGImGKpGDRGpKGERGDQGIP	COL19A1
99919958	4989,21	316,33	EEKAVADTRDQADGSRASVDSGSSEEQGGSSRALVSTLVPLG	PIGR
99920132	199,77	2167,38	LQGLPGTGGppGENGKpGEpGpKGDAGApGApGGKGDAGApGERGpPG	COL3A1
99920387	124,9	6,43	PGPVGpPGSNGPVGEPGPEGPAGNDGTPGRDGAVGERGDRGDPGPAGLPG	COL5A2

Figure 4. *List of the 50 biomarkers which are combined in the DiaPat-CoV-50 test.*

2.2. RESULTS

2.2.1. Classification of urine samples from time point 1 from 228 patients

The previously established **DiaPat-CoV-50** test was applied to urine samples from time point 1 in the first step. **Table 1** and **Table 2** describe the patient cohort used here.

Table 1*Patient characteristics according to quartiles of the DiaPat-CoV-50 test*

Characteristics					*P* value
DiaPat-CoV-50 scoring	<-1.279	>-1.279<-0.296	>-0.296<0.8	>0.8	
Patient number					
All	253	253	253	253	
Male	117	131	144	173	
	20.7%	23.2%	25.5%	30.6%	<0.0001
White ethnicity	210	221	226	233	
	23.6%	24.8%	25.4%	26.2%	n.s.
Smoker					
Yes	78	131	157	191	
	14.0%	23.5%	28.2%	34.3%	<0.0001
Diabetes mellitus	21	43	81	112	<0.0001
	8.2%	16.7%	31.5%	43.6%	
Hypertension	78	131	157	191	<0.0001
	14.0%	23.5%	28.2%	34.3%	
Heart failure	12	28	64	50	<0.0001
	7.8%	18.2%	41.6%	32.5%	
Cancer	10	26	24	46	<0.0001
	9.4%	24.5%	22.6%	43.4%	
Used drugs					
ACE inhibitors	32	53	61	77	
	14.3%	23.8%	27.4%	34.5%	<0.0001
ARB’s	24	49	71	70	
	11.2%	22.9%	33.2%	32.7%	<0.0001
Continuous variables, mean (standard deviation)					

Characteristics					*P* value
Age, years	49.0(16.9)	59.9(16.6)	67.9(15.6)	72.3(12.2)	<0.0001
Systolic blood pressure, mmHg n=981	126.1(18.8)	128.3(19.1)	129.3(20.1)	128.8(22.0)	0.007
Diastolic blodd pressure, mmHg	78.2(11.3)	77.8(12.0)	75.4(11.9)	73.3(12.7)	<0.0001
Heart rate, bpm n=978	79.25 (13.6)	82.29 (15.5)	82.60 (15.8)	84.84 (16.6)	<0.001
eGFR, ml/min/1.73m²	81.7(25.7)	78.0(23.7)	69.8(24.5)	48.9(26.8)	<0.001
BMI n=947	26.8(5.3)	28.3(5.7)	28.3(5.5)	27.5(5.3)	<0.001

Table 2 *Severity of Covid-19 disease according to quartiles of the DiaPat-CoV-50 test*

Characteristics					*P* value
DiaPat-CoV-50 Scoring	<-1.279	>-1.279<-0.296	>-0.296<0.8	>0.8	
Patient number	253	253	253	253	
WHO-Score at baseline n=1012					<0.0001
1	149	27	5	1	
	82.7%	15.0%	2.3%	0.0%	
2	11	4	1	0	
	73.9%	21.7%	4.3%	0.0%	
3	56	87	72	31	
	28.9%	38.8%	23.0%	9.2%	
4	33	116	143	140	
	9.6%	32.0%	34.5%	23.9%	
5	4	16	30	48	
	8.2%	24.5%	38.8%	28.6%	
6	0	3	2	33	
	8.2%	24.5%	38.8%	28.6%	
7					

Characteristics					*P* value
8					
Highest WHO-Score					<0.0001
1	143	26	4	0	
	82.7%	15.0%	2.3%	0.0%	
2	17	5	1	0	
	73.9%	21.7%	4.3%	0.0%	
3	44	59	35	14	
	28.9%	38.8%	23.0%	9.2%	
4	38	126	136	94	
	9.6%	32.0%	34.5%	23.9%	
5	8	24	38	28	
	8.2%	24.5%	38.8%	28.6%	
6	0	3	8	31	
	0.0%	7.1%	19.0%	73.8%	
7	0	1	3	7	
	0.0%	9.1%	27.3%	63.6%	
8	3	9	28	79	
	2.5%	7.6%	23.5%	66.4%	

Table 3 presents the results of the logistic regression analysis, which relates the baseline characteristics to the result. A total of 119 patients died after a median of 10 days (range: 1-49 days) after taken the first urine sample. In 270 patients, the WHO score increased over the course of the observation period (taking into account the worst score during the follow-up period). The 119 deaths are included in these 270 patients.

Table 3. *The influence of the baseline characteristics on the endpoint.*

	Unadjusted Odds ratio (CI)	*P*
Mortality (n=119)		
Gender *(m=1/w=2)*	0,523 (0,346-0,792)	0,0022
Age (+ 10 years)	1,987 (1,689-2,339)	<0,001
BMI (+ 5 kg/m²)	1,024 (0,855-1,226)	0,7956
Comorbidity (+ 1)	1,702 (1,454-1,993)	<0,001
WHO-Score at inclusion (+ 1)	2,405 (1,948-2,971)	<0,001
DiaPat-CoV-50 (+ 1 SD)	2,443 (2,045-2,919)	<0,0001
Worsening of the WHO score (n=270)		
Gender	0,735 (0,511-1,057)	0,0968
Age (+ 10 years)	1,244 (1,117-1,387)	<0,001
BMI (+ 5 kg/m²)	1,005 (0,850-1,187)	0,9567
Comorbidity (+ 1)	1,220 (1,056-1,409)	<0,001
WHO-Score at inclusion (+ 1)	1,106 (0,965-1,269)	0,1484
DiaPat-CoV-50 (+ 1 SD)		

Comorbidity score includes medical history: diabetes (1 point), cancer (2 points) and heart failure (1 point), and heart disease (+1).

Table 4. *Adjustment for covariates, which relates the DiaPat-CoV-50 value at baseline to the result.*

	Odds Ratios für DiaPat-CoV-50 (CI)	*P* value
Mortality(n=1012, e=119)		
Unadjusted	2.443 (2.045-2.919)	<0.0001
Adjusted for		
Gender, Age	2.038 (1.678-2.476)	<0.0001
+ baseline WHO-Score	1.653 (1.335-2.047)	<0.0001
+ BMI + Comorbidity	1.648 (1.327-2.048)	<0.0001
Verschlechterung WHO-Score (n=1012, e=270)		
Unadjusted	1.389 (1.220-1.582)	<0.0001
Adjusted for		
Gender, Age	1.259 (1.084-1.462)	0.0026
+ baseline WHO-Score	1.477 (1.236-1.764)	<0.0001
+ BMI + Comorbidity	1.495 (1.247-1.793)	<0.0001

Odds ratios apply to an increase of one standard deviation in the classifier. Comorbidities = history of high blood pressure, diabetes and/or cancer.

The evaluation was carried out for three different endpoints: death, worsening of the WHO scores and maximum WHO score ≥ 6 (**Table 5**). Significant group discrimination was achieved for all three outcomes. The area under *receiver operating characteristic* (ROC) curve (AUC) was between 0.72 and 0.85.

Table 5 *Discrimination ability of the DiaPat-CoV-50 test*

Endpoint	Number at risk	Number of endpoints	AUC (95%CI)	Cut-off Younden	Sensitivity (95%CI) t	Specificity (95%CI)
Death	1012	119	0.81 (0.78-0.83)	0.47	74.8 (66.0-82.3)	74.5 (71.5-77.3)
Worsening of WHO-Score	1012	270	0.72 (0.69-0.74)	0.04	67.0 (61.1-72.6)	67.3 (63.7-70.6)
Maximum WHO-Score ≥ 6	1012	134	0.83 (0.80-0.85)	0.47	76.9 (69.8-83.0)	77.9 (75.0-80.7)

The DiaPat-CoV-50 test results in consistently higher AUC values compared to the baseline characteristics.

2.2.2. Mortality

The AUC value for the **DiaPat-CoV-50** test is 0.81, for age is 0.77, and for the baseline WHO score is 0.74. A model that includes all 3 variables increases the accuracy of the **DiaPat-CoV-50** test to an AUC of 0.85. This improvement is significant in relation to age and the baseline WHO score.

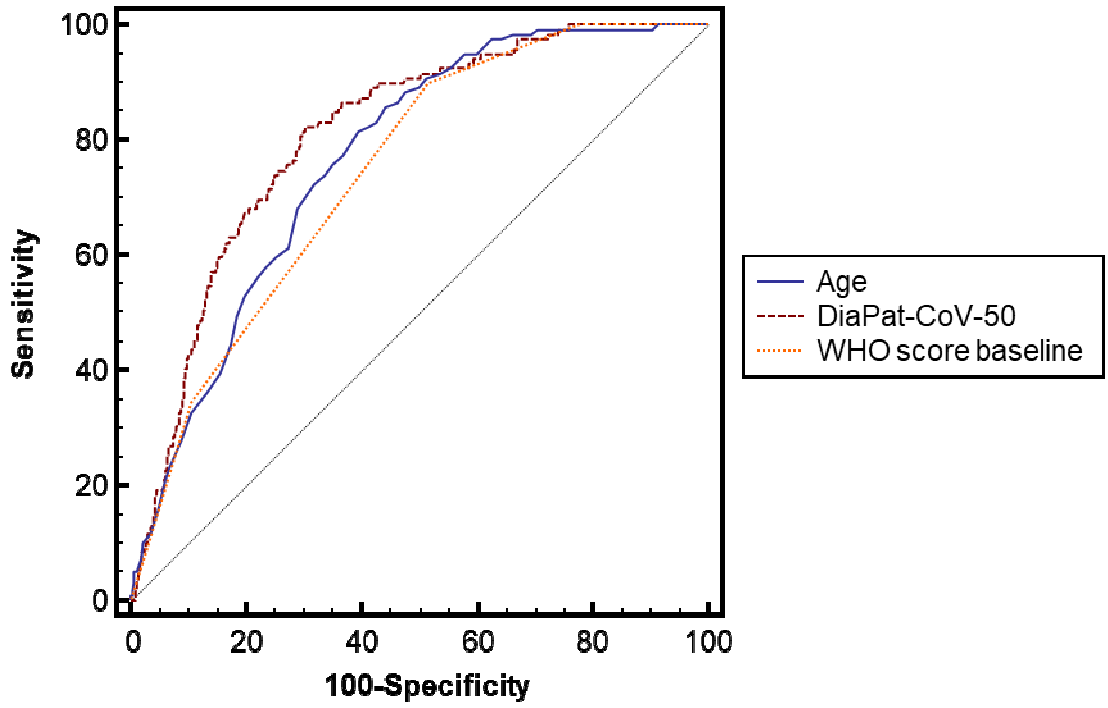

Figure 5. *ROC analysis of the significant parameters age, baseline WHO score, and DiaPat-CoV-50 test for the prediction of death.*

2.2.3. Worsening of the WHO scores

The AUC for predicting the worsening of the WHO score based on the DiaPat-CoV-50 test is 0.72 (95% CI: 0.69-0.74). The AUC for the baseline WHO score is 0.6 (95% CI: 0.57-0.63), the AUC for age is 0.66, and the AUC for a model that includes gender, age and WHO baseline is 0.68 (95% CI: 0.65-0.71). The combination of the three variables increased the AUC to 0.73, a significant improvement in classification based on age or baseline WHO score.

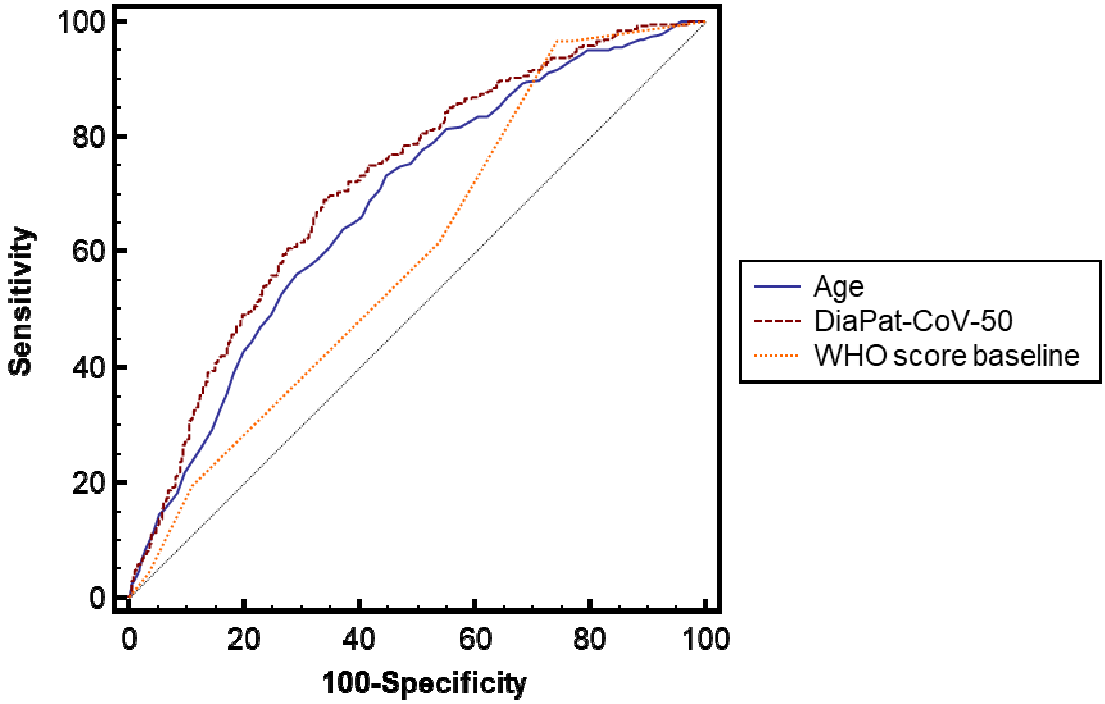

Figure 6. *Performance of the DiaPat-CoV-50 test, age, and baseline WHO score for predicting the worsening of the WHO score.*

2.2.4. Predicting WHO score of 6 or higher

For the prediction of a WHO score of 6 or higher, patients with a baseline WHO score of 6 were excluded (as a prediction is no longer possible). The AUC value for predicting the worsening of the WHO score to 6 or higher based on the **DiaPat-CoV-50** test is 0.83 (95% CI: 0.80-0.85). The AUC value for prediction based on the baseline WHO score is 0.76 (95% CI: 0.73-0.79) and the AUC value for age is 0.73 (95% CI: 0.70-0.76). The combination of the three variables increased the AUC value to 0.86, a significant improvement in the classification based on age or the baseline WHO score.

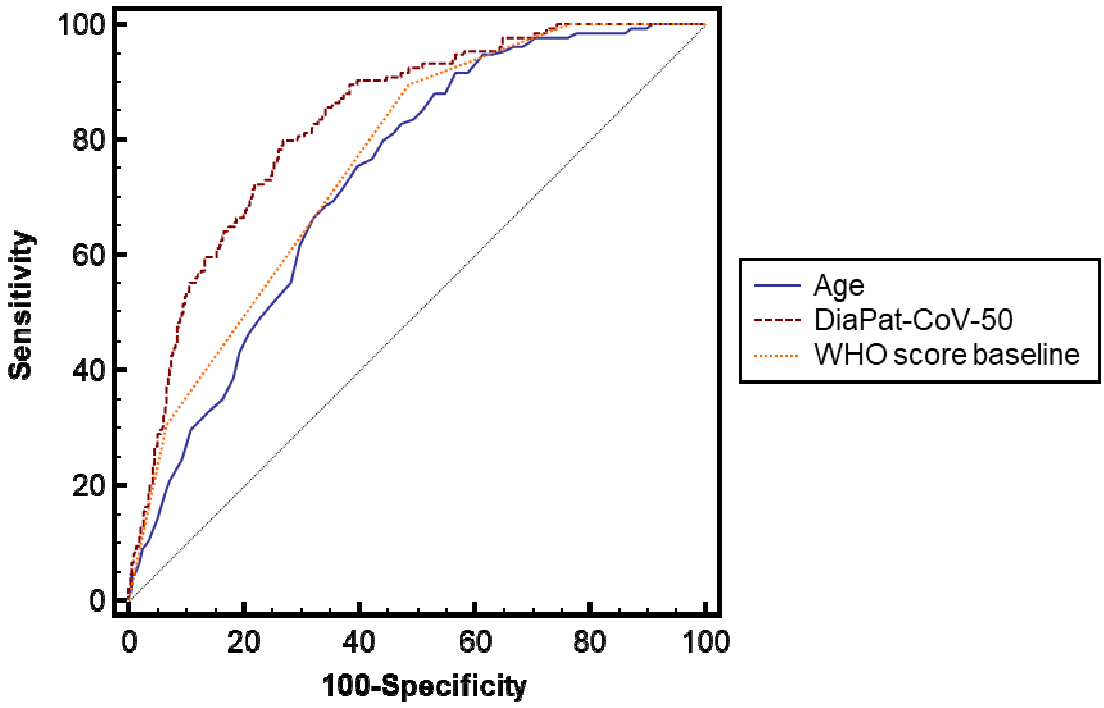

Figure 7. *Performance of the DiaPat-CoV-50 test, age and baseline WHO score for predicting a WHO score> 5.*

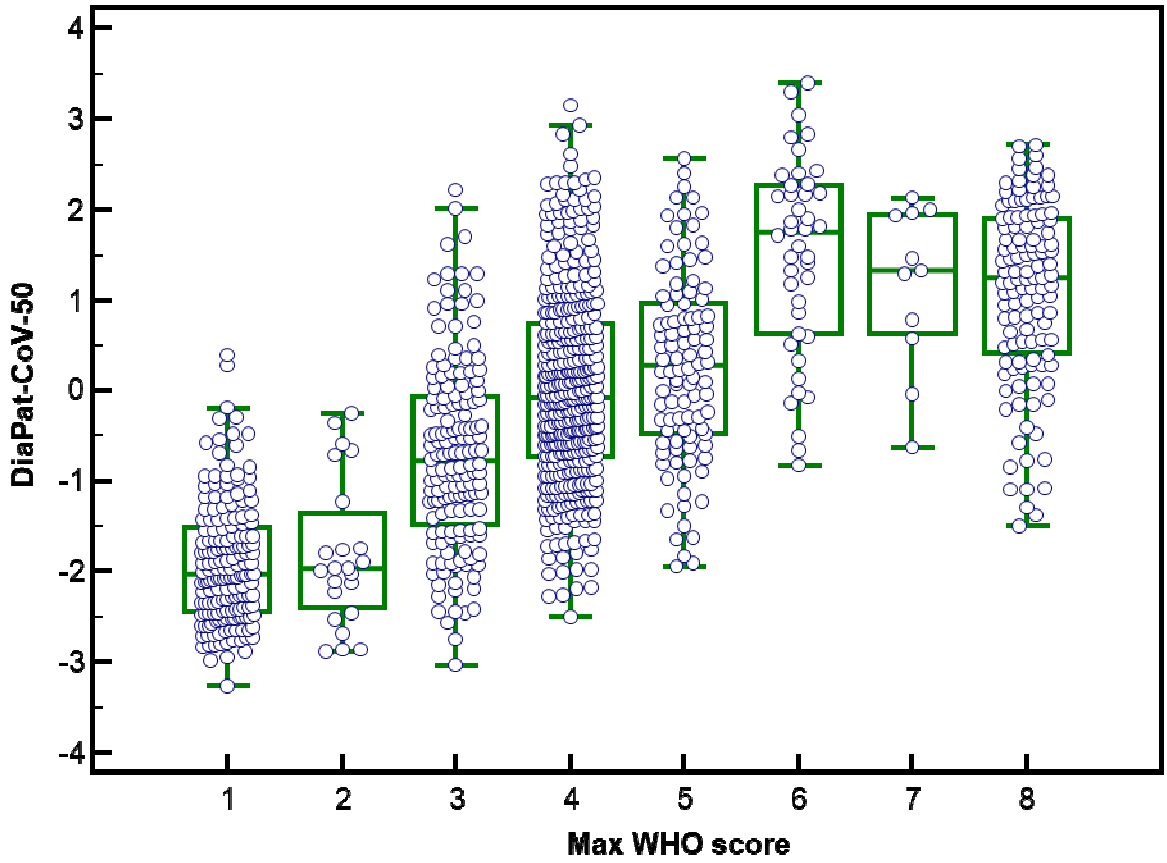

***Figure 8**. Distribution of the DiaPat-CoV-50 test results in the patients stratified according to the highest WHO score. N = 1012. Significance (ANOVA) p> 0.001.*

Distribution of the DiaPat-CoV-50 test in the groups:

Highest WHO score	n	mean DiaPat-CoV-50 value
(1) 1	173	-1.9073
(2) 2	23	-1.8118
(3) 3	152	-0.7065
(4) 4	394	0.03553
(5) 5	98	0.2674
(6) 6	42	1.4951
(7) 7	11	1.1632
(8) 8	119	1.0895

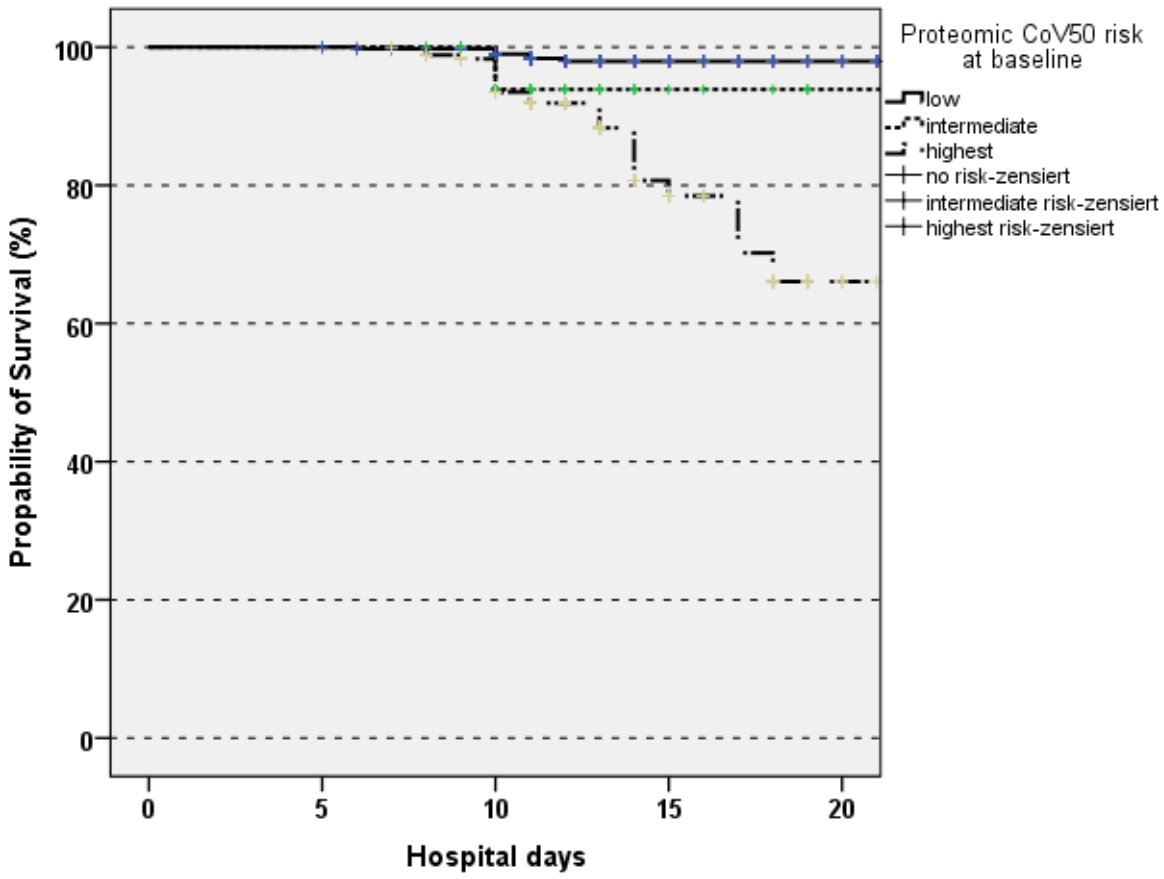

Figure 9. *Survival probability in the three groups, based on the two predetermined cut-off values: 0.04 and 0.47 (low risk = CoV-50 value <0.04, medium risk = 0.04 <CoV-50 value <0.47, high risk = CoV-50 value> 0.47).*

3. Summary

In total, this final evaluation is the full confirmation of the results of the interim evaluation of December 28, 2020, published after peer review in journal THE LANCET eClinicalMedicine (https://doi.org/10.1016/j.eclinm.2021.100883), as expected. All data from the interim evaluation could be confirmed. In the entire cohort of 1012 patients, no significant change was found compared to the interim evaluation.

As also found in the interim evaluation, some covariables show a significant association with the examined endpoints, however

1) In general, this association has a significantly lower value compared to the DiaPat-CoV-50 test, and

2) In addition, there is no pre-specified cut-off for these covariates (which is defined for the DiaPat-CoV-50 test), an essential prerequisite for clinical implementation.