

**High-tech parameters for the evaluation of signs and symptoms of dry eye disease: identification of clinical cut-offs and agreement with low-tech tests**

**Supplementary Materials**

Paolo Fogagnolo<sup>\*1</sup>, Pasquale Aragona<sup>2</sup>, Alfonso Strianese<sup>3</sup>, Edoardo Villani<sup>4,5</sup>, Giuseppe Giannaccare<sup>6</sup>, Vincenzo Orfeo<sup>7</sup>, Valentina Mirisola<sup>8</sup> and Rita Mencucci<sup>9</sup> on behalf of the Italian Dry Eye Study Group<sup>§</sup>

<sup>§</sup>Italian Dry Eye Study Group: Valentino De Ruvo, Silvia Sonego, Chiara Quisisana, Luca Mario Rossetti (Università degli Studi di Milano); Elisa Imelde Postorino, Claudia Azzaro (University of Messina).

<sup>1</sup>Health Sciences Department, Università degli Studi di Milano, Milan, Italy

<sup>2</sup>Department of Biochemical Sciences, Section of Ophthalmology, University of Messina, Messina, Italy

<sup>3</sup>Eye Clinic, ASST Santi Paolo E Carlo, University of Milan, Milan, Italy

<sup>4</sup>Department of Clinical Science and Community Health, University of Milan, Milan, Italy

<sup>5</sup>Eye Clinic San Giuseppe Hospital, IRCCS Multimedica, Milan, Italy

<sup>6</sup>Department of Ophthalmology, University Magna Graecia of Catanzaro, Catanzaro, Italy

<sup>7</sup>Unità Operativa di Oculistica Clinica Mediterranea, Naples, Italy

<sup>8</sup>Polistudium SRL, Milan, Italy

<sup>9</sup>Department of Neurosciences, Psychology, Drug Research, and Child Health, Eye Clinic, University of Florence, AOU Careggi, Florence, Italy

**\*Corresponding Author details:**

Paolo Fogagnolo, MD

paolo.fogagnolo@unimi.it

**Supplementary Table 1. Paired test analysis for NIKBUT-I and T-BUT, by visit**

	T-BUT	NIKBUT-I	p-value
Baseline (N=144)	4.4 ( $\pm 1.6$ )	5.5 ( $\pm 4.2$ )	0.004
15 days (N=144)	5.5 ( $\pm 2.4$ )	6.0 ( $\pm 3.8$ )	0.137
45 days (N=145)	6.3 ( $\pm 2.6$ )	6.7 ( $\pm 3.6$ )	0.289

Multiple regression analysisModel #1: multiple regression analysis, stepwise method, total population, Baseline ODSI, N=118

Dependent variable: Baseline OSDI

Independent variables: Baseline Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- Baseline Tbut, coeff. -2.7, SE 0.8, **p<0.001**
- Baseline Schirmer test, coeff. 0.7, SE 0.2, **p<0.001**

Model #2: multiple regression analysis, stepwise method, total population, 15-days ODSI, N=118

Dependent variable: 15 days Baseline

Independent variables: 15 days Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- 15 days Tbut, coeff. -0.7, SE 0.3, **p=0.033**

[Model #3: multiple regression analysis, stepwise method, total population, 45-days ODSI, N=118](#)

Dependent variable: 45 days Baseline

Independent variables: 45 days Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- 45-days Nikbut i, coeff. -0.5, SE 0.2, **p=0.017**
- 45-days Schirmer test, coeff. -0.3, SE 0.1, **p=0.014**

[Model #4: multiple regression analysis, stepwise method, patients with allergy, Baseline ODSI, N=34](#)

Dependent variable: Baseline OSDI

Independent variables: Baseline Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- Baseline Schirmer test, coeff. 0.7, SE 0.3, **p=0.016**

[Model #5: multiple regression analysis, stepwise method, patients with allergy, 15 days ODSI, N=34](#)

Dependent variable: 15 days OSDI

Independent variables: 15 days Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- no variables

[Model #6: multiple regression analysis, stepwise method, patients with allergy, 45 days ODSI, N=34](#)

Dependent variable: 45 days OSDI

Independent variables: 45 days Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- no variables

[Model #7: multiple regression analysis, stepwise method, patients with blefaritis,](#)

[Baseline ODSI, N=28](#)

Dependent variable: Baseline OSDI

Independent variables: Baseline Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- Baseline corneal staining, coeff. -9.0, SE 3.8, **p=0.027**

[Model #8: multiple regression analysis, stepwise method, patients with blefaritis, 15-days ODSI, N=28](#)

Dependent variable: 15 days OSDI

Independent variables: 15 days Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- 15 days EFRON, coeff. -6.8, SE 3.1, **p=0.038**

[Model #9: multiple regression analysis, stepwise method, patients with blefaritis, 45 days ODSI, N=28](#)

Dependent variable: 45 days OSDI

Independent variables: 45 days Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

45-days meibography, coeff. -7.2, SE 3.2, **p=0.035**

[Model #10: multiple regression analysis, stepwise method, patients with post cataract surgery, Baseline ODSI, N=49](#)

Dependent variable: Baseline OSDI

Independent variables: Baseline Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron, Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- Baseline Schirmer, coeff. -1.2, SE 0.4, **p=0.005**

[Model #11: multiple regression analysis, stepwise method, patients with post cataract, 15 days ODSI, N=49](#)

Dependent variable: 15 days OSDI

Independent variables: 15 days Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron,

Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

- 15-days Tbut, coeff. -0.7, SE 0.3, **p=0.030**

Model #12: multiple regression analysis, stepwise method, patients with post cataract,  
45 days OSDI, N=49

Dependent variable: 45 days OSDI

Independent variables: 45 days Tbut, Nikbut a, Nikbut i, Nikbut class, hyperemia, meniscus, Efron,  
Schirmer, Conjunctivo calasis, meibography, corneal staining

Variables retained in the model:

45-days Nikbut a, coeff. -0.7, SE 0.2, **p=0.003**

Variation of NIKBUT i, NIKBUT a and TBUT compared with baseline

Delta (NIKBUT-I visit 3 – NIKBUT-I baseline), patients ameliorated by 7+ or not = 0.8 ( $\pm 5.6$ )

Delta (NIKBUT-a visit 3 – NIKBUT-a baseline), patients ameliorated by 7+ or not = -0.3 ( $\pm 6.0$ )

Comparison between delta NIKBUT-I and delta NIKBUT-a, paired Student's test, p=0.097

Delta (NIKBUT-I visit 3 – NIKBUT-I baseline), patients ameliorated by 7+ or not = 0.8 ( $\pm 5.6$ )

Delta (T-BUT visit 3 – T-BUT baseline), patients ameliorated by 7+ or not = 0.5 ( $\pm 3.3$ )

Comparison between delta NIKBUT-I and delta T-BUT, paired Student's test, p=0.619

Delta (NIKBUT-a visit 3 – NIKBUT-a baseline), patients ameliorated by 7+ or not = -0.3 ( $\pm 6.0$ )

Delta (T-BUT visit 3 – T-BUT baseline), patients ameliorated by 7+ or not = 0.5 ( $\pm 3.3$ )

Comparison between delta NIKBUT-a and delta T-BUT, paired Student's test, p=0.338