

## STUDY REPORT SUMMARY

### ASTRAZENECA PHARMACEUTICALS

**FINISHED PRODUCT:** Not applicable

**ACTIVE INGREDIENT:** Not applicable

**Study No:** NIS-CEU-DUM-2008/2

PANORAMA. Quality of Life and Treatment Satisfaction of People with Type 2 Diabetes: A European Survey

**Developmental Phase:** Not applicable

**Study Completion Date:** 23/03/2010

**Date of Report:** 12/11/2010

### OBJECTIVES:

Primary Objective:

- *Evaluate diabetes-related QoL and treatment satisfaction of patients with T2DM treated with diet, oral agents and/or insulin.*

Secondary Objectives:

- *Compare patient-reported measures (DTSQ, ADDQoL, HFS-II (worry subscale) and EQ-5D) between diabetes treatment subgroups (diet only, OADs and/or insulin) and between categories of HbA<sub>1c</sub>.*
- *Evaluate hypoglycaemia-specific health utility as well as diabetes-specific and overall health utility through the use of the worry subscale of the HFS-II, ADDQoL and EQ-5D instruments, respectively.*
- *Evaluate association of patient-reported measures with diabetes control and CV risk factors.*
- *Evaluate diabetes-related QoL as a function of patient treatment satisfaction.*
- *Correlate DTSQ scores with health utility measures in specific patient subgroups.*

- *Evaluate changes in healthcare resource utilization in relation to treatment satisfaction and rate of hypoglycaemia (e.g. emergency departments and hospitalisations).*
- *Determine compliance to evidence-based clinical guidelines for diabetes management by physicians.*
- *Compare study outcomes and clinical practice between participating countries.*
- *Compare the physician's perception of patients' satisfaction with the patient treatment satisfaction.*

## **METHODS:**

Observational, multicentre, multinational, cross-sectional study conducted in 9 European countries (Belgium, France, Germany, Greece, Italy, The Netherlands, Spain, Turkey and United Kingdom).

Disease and treatment variables as well as patient-related outcomes were collected at the study visit and other important information was obtained retrospectively from clinical records. HbA1c was assessed during the study visit.

A representative sample of physicians with access to patients with T2D was selected in each country.

Patients with T2D were then randomly or consecutively selected from these physician practices.

Key inclusion criteria:

- Patients aged  $\geq 40$  years
- Diagnosis of T2D for  $>1$  year prior to study entry
- Available medical record at the clinic of  $>1$  year

Patients included were on dietary/exercise advice, oral antidiabetes drugs (OADs) and/or injectables (insulin and/or glucagon-like peptide (GLP)-1 receptor agonists).

At the study visit, information was collected from participating patients and their medical records for the past 1 to 2 years.

Data collected included patient socio-demographics, biological measures, PROs, disease-related variables including glycosylated haemoglobin (HbA1c) using a standardised method in all practices (Bayer's A1Cnow device certified by US National Glycohemoglobin Standardization Program), health-economic variables, physician-reported endpoints and physician socio-demographics.

Patients completed the following questionnaires in their preferred language:

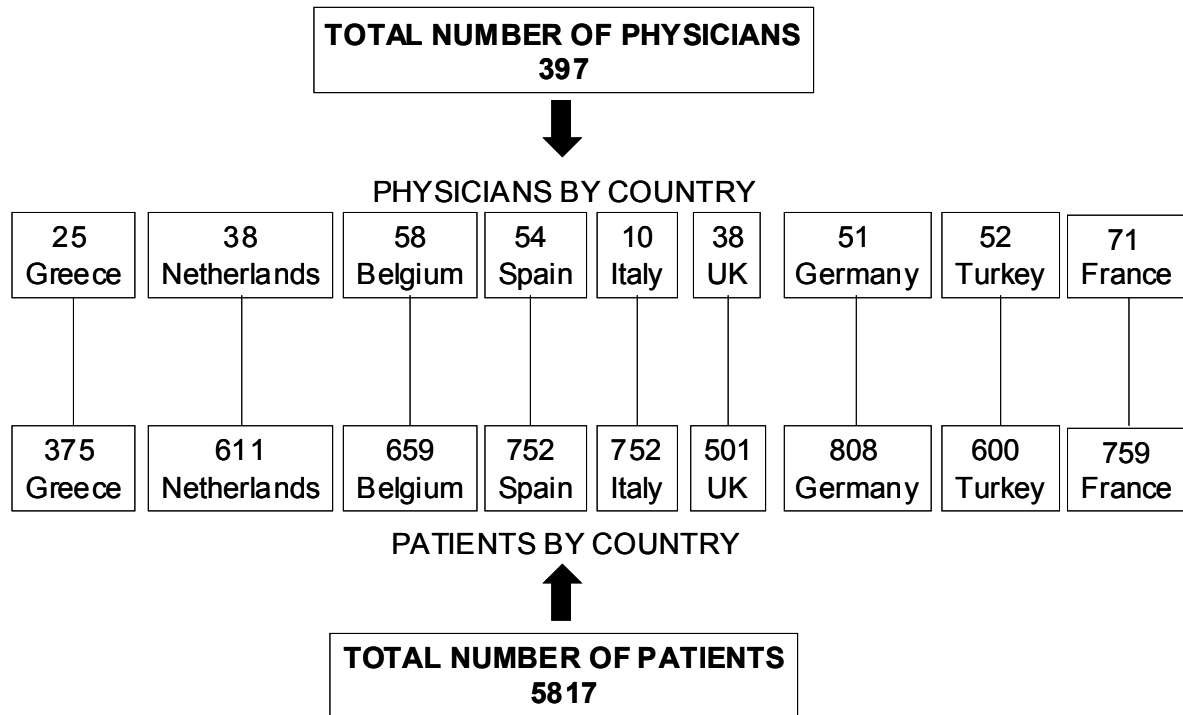
- European Quality of Life-5 Dimensions (EQ-5D).
- Audit of Diabetes-Dependent Quality of Life (ADDQoL).
- Diabetes Treatment Satisfaction Questionnaire (DTSQ).
- Hypoglycaemia Fear Survey (HFS-II) Worry Subscale.

Patient-reported frequencies of severe and non-severe hypoglycaemic episodes in the past year were examined.

- Severe hypoglycaemic episodes were defined as symptomatic episodes requiring external assistance due to severe impairment in consciousness or behaviour and prompt recovery after glucose or glucagon administration.
- Number of severe hypoglycaemic episodes during the last 12 months was reported.
- Number of non-severe hypoglycaemic episodes on average per month was reported during the last 12 months.

**RESULTS:**

**-Physicians' and patients' disposition**



**-Patient social and demographic characteristics**

<b>Age</b>	N	Mean (SD)
	5816	65.9 (10.4)
<b>Sex</b>	N=5816	%
Female	2693	46.3
Male	3123	53.7
<b>Living alone</b>	N=5813	%
	1287	22.1
<b>Age of leaving full-time education</b>	N=4570	%
<18 years old	3196	69.9
<b>University degree</b>	N=5813	%
	570	9.8
<b>Patient's occupation</b>	N=5793	%
Employed	1185	20.5
Homemaker	804	13.9
Student	1	0.0
Retired	3215	55.5
Sickleave	185	3.2
Unemployed	250	4.3
Other	153	2.6
<b>Smoking status</b>	N=5816	%
Never	3167	54.5
Former smoker	1815	31.2
Current smoker	834	14.3
<b>Smoking status among participants &lt;65 years old</b>	N=2650	%
Never	1300	49.1
Former smoker	793	29.9
Current smoker	557	21.0
<b>Smoking status among participants ≥65 years old</b>	N=3166	%
Never	1867	59.0
Former smoker	1022	32.3
Current smoker	277	8.7
<b>Smoking status among women</b>	N=2693	%
Never	1960	72.8
Former smoker	433	16.1
Current smoker	300	11.1
<b>Smoking status among men</b>	N=3122	%
Never	1206	38.6
Former smoker	1382	44.3
Current smoker	534	17.1
<b>Number of years since stopped smoking</b>	No.	Mean (SD)
	1812	17.5 (12.2)
<b>Alcohol consumption (units*/week)</b>	N	Mean (SD)
Women	2693	2.5 (10.9)
Men	3122	8.2 (18.3)
<b>Physical activity</b>	N=5816	%
None	1496	25.7
Light	2680	46.1
Intense(**) 1 to 2 times per week	1041	17.9
Intense(**) ≥ times per week	599	10.3

(\*) 1 unit: 250 ml beer (4% strength) or a small glass (80 ml) of wine or champagne (12% strength) or 25 ml spirits (40% strength)

(\*\*) Intense physical activity: for at least 20min

**-Disease characteristics and comorbidity**

<b>Average duration of diabetes type II</b>	N	Mean (SD)
	5817	8.9 (7.1)
<b>Duration of diabetes type II</b>	N=5817	%
Less than 5 years	2019	34.7
>=5 & < 9 years	1557	26.8
>=9 years	2241	38.5
<b>Years on insulin treatment</b>	N	Mean (SD)
	997	5.9 (5.5)
<b>Microvascular complications</b>	N=5817	%
Chronic diabetic polyneuropathy	1655	28.5
- Asymptomatic	833	14.3
- Symptomatic	297	5.1
Autonomic neuropathy	537	9.2
Diabetic retinopathy	212	3.6
Diabetic nephropathy	571	9.8
- Micro-albuminuria	643	11.1
- Proteinuria	449	7.7
- Renal insufficiency	131	2.3
- Dialysis	166	2.9
- Dialysis	6	0.1
Prior treatment with photocoagulation	173	3.0
<b>Macrovascular complications</b>	N=5817	%
Coronary Heart Disease	1427	24.5
Cerebrovascular disease	989	17.0
Peripheral vascular disease	272	4.7
Amputation	414	7.1
Amputation	27	0.5
<b>Other complications</b>	N=5817	%
Congestive Heart Failure	208	3.6
Erectile dysfunction among men	743	23.8
Depressive disorders	800	13.8
Other mood disorders	352	6.1
Sleep disorders	532	9.1
Non alcoholic steatohepatitis (NAHS) and/or fatty liver disease	833	14.3
Gout	249	4.3
Gout	269	4.6

<b>Past or present genito-urinary infections</b>		
Among women	N=2693	%
- Cystitis	524	19.5
- Pyelonephritis	46	1.7
- Genital mycotic/yeast infections	138	5.1
Among men	N=3123	%
- Cystitis	128	4.1
- Pyelonephritis among men	25	0.8
- Genital mycotic/yeast infections	56	1.8
	N	Mean (SD)
No. of mycotic/yeast infections in the past 12 months among women	2693	0.1 (0.7)
No of mycotic/yeast infections occurred in the past 12 months among men	3123	0.0 (0.4)

<sup>1</sup> Nephropathy, new variable created if in the in the CRF was checked micro-albuminuria, proteinuria, renal insufficiency or dialysis

**-Clinical and biological measures**

<b>ANTHROPOMETRIC DATA</b>		
	N=5815	Mean (SD)
<b>Height (cm)</b>		166.5 (9.6)
<b>Weight (Kg)</b>		83.9 (17.2)
<b>Body Mass Index (Kg/m<sup>2</sup>)</b>	N=5815	%
Normal: bmi<25	901	15.5
Overweight: bmi $\geq$ 25 & bmi<30	2264	38.9
Obese: bmi $\geq$ 30	2650	45.6
	N	Mean (SD)
<b>Waist circumference in women (cm)</b>	2682	102.2 (14.8)
<b>Waist circumference in men (cm)</b>	3120	105.2 (13.1)
<b>BLOOD PRESSURE</b>		
<b>Hypertension</b>	N=5815	%
Systolic BP<130 mmHg or Diastolic BP<80mm Hg	1145	19.7
<b>SELF MONITORING BLOOD GLUCOSE (SMBG)</b>		
<b>N° patients doing SMBG</b>	N=5811	%
	2793	48.1
<b>N° of measurements on average per week during the past 3 months:</b>	N	Mean (SD)
Fasting plasma glucose measurements	2792	3.1 (2.9)
Preprandial glucose measurements	2789	3.2 (4.7)
Postprandial glucose measurements	2790	2.4 (3.6)
<b>N° of total measurements per week because of symptoms</b>	N=2784	%
None	2025	72.7
1	339	12.2
2	217	7.8
3	77	2.8
4	43	1.5
$\geq$ 5	83	3.0
<b>N° of total SMBG measurements to self adjust insulin therapy among those using insulin</b>	N=997	%
None	392	39.3
1	85	8.5
2	72	7.2
3	40	4.0
4	39	3.9
$\geq$ 5	369	37.0

**-Diabetes treatment**

<b>DIABETES TREATMENT</b>	<b>N=5814</b>	<b>%</b>
<b>ONLY DIET AND/OR EXERCISE</b>	<b>575</b>	<b>9.9</b>
<b>INSULIN</b>	<b>1172</b>	<b>20.2</b>
<b>Only insulin</b>	<b>404</b>	<b>6.9</b>
<b>Rapid-acting insulin</b>	<b>364</b>	<b>6.3</b>
Insulin lispro	107	1.8
Insulin aspart	192	3.3
Insulin glulisine	65	1.1
<b>Short-acting insulin</b>	<b>141</b>	<b>2.4</b>
<b>Intermediate-acting insulin</b>	<b>180</b>	<b>3.1</b>
<b>Long-acting insuline</b>	<b>611</b>	<b>10.5</b>
Insulin glargine	455	7.8
Insulin detemir	156	2.7
<b>Fixed combinations</b>	<b>286</b>	<b>4.9</b>
<b>GLP-1_ANALOGS</b>	<b>54</b>	<b>0.9</b>
<b>Exenatide</b>	<b>50</b>	<b>0.9</b>
<b>Liraglutide</b>	<b>4</b>	<b>0.1</b>

**-ADD-QoL weighted impact score**

	<b>N</b>	<b>Mean (SD)</b>
ADD-QoL Average Weighted Impact Score*	5683	-1.7 (1.8)



**-DTSQ**

DTSQ <sub>physicians</sub>			DTSQ <sub>patients</sub>		
<b>Satisfaction with treatment</b>	<b>N=5674</b>	<b>%</b>	<b>Satisfaction with treatment</b>	<b>5531</b>	<b>%</b>
1 (Very dissatisfied)	36	0.6	1 (Very dissatisfied)	44	0.8
2	82	1.4	2	56	1
3	175	3.1	3	89	1.6
5	514	9.1	5	334	6.4
5	1229	21.7	5	702	12.7
6	2126	37.5	6	1511	27.3
7 (Very satisfied)	1512	26.6	7 (Very satisfied)	2775	50.2
<b>Unacceptably high glucose</b>	<b>N=5675</b>	<b>%</b>	<b>Unacceptably high glucose</b>	<b>5436</b>	<b>%</b>
1 (None of the time)	1664	29.3	1 (None of the time)	1669	30.7
2	1330	23.4	2	928	17.1
3	861	15.2	3	789	14.5
4	666	11.7	4	703	12.9
5	622	11	5	635	11.7
6	398	7	6	415	7.6
7 (Most of the time)	134	2.4	7 (Most of the time)	297	5.5
<b>Unacceptably low glucose</b>	<b>N=5668</b>	<b>%</b>	<b>Unacceptably low glucose</b>	<b>5362</b>	<b>%</b>
1 (None of the time)	2412	42.6	1 (None of the time)	2478	46.2
2	1530	27	2	994	18.5
3	809	14.3	3	688	12.8
4	448	7.9	4	515	9.6
5	248	4.4	5	312	5.8
6	171	3	6	193	3.6
7 (Most of the time)	50	0.9	7 (Most of the time)	182	3.4
<b>Convenience</b>	<b>N=5675</b>	<b>%</b>	<b>Convenience</b>	<b>5481</b>	<b>%</b>
1 (Very inconvenient)	38	0.7	1 (Very inconvenient)	79	1.4
2	76	1.3	2	69	1.3
3	226	4	3	156	2.8
4	564	9.9	4	396	7.2
5	1271	22.4	5	716	13.1
6	2031	35.8	6	1489	27.2
7 (Very convenient)	1469	25.9	7 (Very convenient)	2576	47
<b>Flexibility</b>	<b>N=5675</b>	<b>%</b>	<b>Flexibility</b>	<b>5455</b>	<b>%</b>
1 (Very inflexible)	55	1	1 (Very inflexible)	110	2
2	97	1.7	2	106	1.9
3	297	5.2	3	199	3.6
4	701	12.4	4	531	9.7
5	1327	23.4	5	767	14.1
6	1937	34.1	6	1435	26.3
7 (Very flexible)	1261	22.2	7 (Very flexible)	2307	42.3
<b>Understanding of diabetes</b>	<b>N=5673</b>	<b>%</b>	<b>Understanding of diabetes</b>	<b>5490</b>	<b>%</b>
1 (Very dissatisfied)	43	0.8	1 (Very dissatisfied)	102	1.9
2	76	1.3	2	105	1.9
3	249	4.4	3	207	3.8
5	737	13	5	540	9.8
5	1457	25.7	5	907	16.5
6	1997	35.2	6	1554	28.3
7 (Very satisfied)	1114	19.6	7 (Very satisfied)	2075	37.8
<b>Willing to recommend to someone else</b>	<b>N=5669</b>	<b>%</b>	<b>Willing to recommend to someone else</b>	<b>5432</b>	<b>%</b>
1 (No, I would definitely not recommend the treatment)	95	1.7	1 (No, I would definitely not recommend the treatment)	65	1.2
2	81	1.4	2	91	1.7
3	155	2.7	3	353	6.5
4	511	9	4	585	10.8
5	1188	21	5	1215	22.4
6	2061	36.4	6	2850	52.5
7 (Yes, I would definitely recommend the treatment)	1578	27.8	7 (Yes, I would definitely recommend the treatment)	2850	52.5
<b>Satisfied to continue with treatment</b>	<b>N=5674</b>	<b>%</b>	<b>Satisfied to continue with treatment</b>	<b>5483</b>	<b>%</b>
1 (Very dissatisfied)	31	0.5	1 (Very dissatisfied)	53	1
2	58	1	2	64	1.2
3	161	2.8	3	91	1.7
5	444	7.8	5	313	5.7
5	1021	18	5	561	10.2
6	2052	36.2	6	1363	24.9
7 (Very satisfied)	1907	33.6	7 (Very satisfied)	3038	55.4
	<b>N</b>	<b>mean (SD)</b>		<b>N</b>	<b>mean (SD)</b>
<b>DTSQ total score for the physicians</b>	<b>5639</b>	<b>27.8 (5.9)</b>	<b>DTSQ total score for the patients</b>	<b>5300</b>	<b>29.8 (6.1)</b>

**-HFS II Worry subscale**

	N	%		N	%
<b>I'm worried not realizing blood sugar levels had dropped</b>	N=5463	%	<b>I'm worried making mistake or having an accident</b>	N=5394	%
Never	2391	43.8	Never	3412	63.3
Almost never	1362	24.9	Almost never	917	17
Sometimes	1088	19.9	Sometimes	542	10
Frequently	395	7.2	Frequently	277	5.1
Almost always	227	4.2	Almost always	246	4.6
<b>I'm worried not having food, fruit or juice available</b>	N=5461	%	<b>I'm worried getting a bad evaluation/being criticized</b>	N=5413	%
Never	2702	49.5	Never	3664	67.7
Almost never	1302	23.8	Almost never	938	17.3
Sometimes	870	15.9	Sometimes	507	9.4
Frequently	368	6.7	Frequently	196	3.6
Almost always	219	4	Almost always	108	2
<b>I'm worried passing out in public</b>	N=5444	%	<b>I'm worried difficulty thinking clearly/respble.for others</b>	N=5417	%
Never	3534	64.9	Never	3298	60.9
Almost never	897	16.5	Almost never	1014	18.7
Sometimes	507	9.3	Sometimes	606	11.2
Frequently	308	5.7	Frequently	281	5.2
Almost always	198	3.6	Almost always	218	4
<b>I'm worried to embarrass myself/friends in social situations</b>	N=5451	%	<b>I'm worried feeling lightheaded or dizzy</b>	N=5438	%
Never	3678	67.5	Never	2404	44.2
Almost never	888	16.3	Almost never	1364	25.1
Sometimes	493	9	Sometimes	980	18
Frequently	241	4.4	Frequently	443	8.1
Almost always	151	2.8	Almost always	247	4.5
<b>I'm worried having hypoglycemic episode while alone</b>	N=5447	%	<b>I'm worried accidentally injuring myself or others</b>	N=5422	%
Never	2960	54.3	Never	3557	65.6
Almost never	1033	19	Almost never	867	16
Sometimes	728	13.4	Sometimes	500	9.2
Frequently	416	7.6	Frequently	278	5.1
Almost always	310	5.7	Almost always	220	4.1
<b>I'm worried appearing stupid or drunk</b>	N=5437	%	<b>I'm worried perm. injury or damage to health/body</b>	N=5431	%
Never	3618	66.5	Never	2989	55
Almost never	862	15.9	Almost never	961	17.7
Sometimes	523	9.6	Sometimes	748	13.8
Frequently	270	5	Frequently	433	8
Almost always	164	3	Almost always	300	5.5
<b>I'm worried losing control</b>	N=5442	%	<b>I'm worried low blood sugar interfering/imprt.things</b>	N=5423	%
Never	3393	62.3	Never	3176	58.6
Almost never	957	17.6	Almost never	1051	19.4
Sometimes	550	10.1	Sometimes	645	11.9
Frequently	315	5.8	Frequently	336	6.2
Almost always	227	4.2	Almost always	215	4
<b>I'm worried no one to help during a hypo episode</b>	N=5447	%	<b>I'm worried becoming hypoglycemic during sleep</b>	N=5427	%
Never	2889	53	Never	3330	61.4
Almost never	1065	19.6	Almost never	882	16.3
Sometimes	727	13.3	Sometimes	601	11.1
Frequently	407	7.5	Frequently	337	6.2
Almost always	359	6.6	Almost always	277	5.1
<b>I'm worried having a hypo episode while driving</b>	N=5352	%	<b>I'm emotionally upset/difficult to deal with</b>	N=5435	%
Never	3729	69.7	Never	3150	58
Almost never	751	14	Almost never	983	18.1
Sometimes	427	8	Sometimes	666	12.3
Frequently	218	4.1	Frequently	382	7
Almost always	227	4.2	Almost always	254	4.7

HFS total score	N	Mean (SD)
	4870	13.3 (15.4)

**-EuroQoL 5-Dimensions (EQ-5D)**

<b>EQ5D</b>	N=5722	%
<b>Mobility</b>		
No problem	3710	64.8
Some problems	1852	32.4
Extreme problems	28	0.5
Unknown	132	2.3
<b>Self-care</b>		
No problem	4961	86.7
Some problems	547	9.6
Extreme problems	55	1
Unknown	159	2.8
<b>Usual activities</b>		
No problem	4124	72.1
Some problems	1313	22.9
Extreme problems	141	2.5
Unknown	144	2.5
<b>Pain/discomfort</b>		
No problem	2673	46.7
Some problems	2500	43.7
Extreme problems	391	6.8
Unknown	158	2.8
<b>Anxiety/depression</b>		
No problem	3371	58.9
Some problems	1905	33.3
Extreme problems	301	5.3
Unknown	145	2.5

## - Patient reported outcomes in treatment subgroups

QoL	Treatment Subgroup*	N	CRUDE ANALYSIS		ADJUSTED ANALYSIS**		ADJUSTED ANALYSIS***	
			Mean difference of scales scores with respect to AODs (95% CI)	P value	Mean difference of scales scores with respect to AODs (95% CI)	P value	Mean difference of scales scores with respect to AODs (95% CI)	P value
ADDQoL	Diet	635	0.14 (-0.00 to 0.28)	P= 0.056	-0.03 (-0.19 to 0.13)	P=0.688	-0.04 (-0.20 to 0.12)	P=0.599
	Injectables	1220	0.76 ( 0.87 to 0.65)	P<0.001	0.59 ( 0.72 to 0.47)	P<0.001	0.59 ( 0.72 to 0.46)	P<0.001
DTSQ <sub>physician</sub>	Diet	635	1.64 (1.19 to 2.09)	P<0.001	1.30 ( 0.80 to 1.80)	P<0.001	1.30 ( 0.81 to 1.80)	P<0.001
	Injectables	1220	-3.15 (-3.48 to -2.81)	P<0.001	-2.94 (-3.33 to -2.54)	P<0.001	-2.95 (-3.35 to -2.55)	P<0.001
DTSQ <sub>patient</sub>	Diet	635	0.35 (-0.18 to 0.88)	P=0.196	-0.19 (-0.78 to 0.40)	P=0.523	-0.21 (-0.80 to 0.38)	P=0.491
	Injectables	1220	-2.25 (-2.64 to -1.87)	P<0.001	-2.17 (-2.64 to -1.71)	P<0.001	-2.16 (-2.63 to -1.69)	P<0.001
HFS II	Diet	635	-1.37 (-2.73 to -0.00)	P=0.050	-0.94 (-2.42 to 0.55)	P=0.218	-0.91 (-2.40 to 0.38)	P=0.233
	Injectables	1220	5.74 ( 4.73 to 6.75)	P<0.001	5.01 ( 3.82 to 6.19)	P<0.001	4.99 ( 3.79 to 6.18)	P<0.001
EuroQoL	Diet	635	1.86 ( 0.32 to 3.40)	P=0.018	0.89 (-0.80 to 2.58)	P=0.301	0.90 (-0.79 to 2.59)	P=0.297
	Injectables	1220	-5.92 (-7.08 to -4.77)	P<0.001	-4.58 (-5.93 to -3.22)	P<0.001	-4.60 (-5.97 to -3.24)	P<0.001

(\*) Reference group: AODs, N=3959

(\*\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country.

(\*\*\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country; and for physician's characteristics: main specialty, main location of clinical activities, practice setting, type of practice, practice location and number of patients with diabetes/week

## - QoL and treatment satisfaction, fear of hypoglycaemia and health status in HbA1c categories

	HbA <sub>1c</sub> *	N	CRUDE ANALYSIS	ADJUSTED ANALYSIS**	ADJUSTED ANALYSIS***
			Mean difference of scales scores with respect to HbA <sub>1c</sub> <7% (95% CI); P value	Mean difference of scales scores with respect to HbA <sub>1c</sub> <7% (95% CI); P value	Mean difference of scales scores with respect to HbA <sub>1c</sub> <7% (95% CI); P value
ADDQoL	≥ 7.0%	2173	-0.44 (-0.53 to -0.35); P<0.001	0.28 (-0.39 to -0.18); P<0.001	-0.29 (-0.39 to -0.19); P<0.001
DTSQ <sub>physician</sub>	≥ 7.0%	2173	-3.23 (-3.51 to -2.95); P<0.001	-2.74 (-3.05 to -2.43); P<0.001	-2.74 (-3.06 to -2.43); P<0.001
DTSQ <sub>patient</sub>	≥ 7.0%	2173	-2.27 (-2.59 to -1.95); P<0.001	-1.93 (-2.30 to -1.56); P<0.001	-1.92 (-2.29 to -1.55); P<0.001
HFS II	≥ 7.0%	2173	2.61 ( 1.76 to 3.46); P<0.001	1.52 (0.57 to 2.48); P=0.002	1.56 (0.60 to 2.51); P=0.001
EuroQoL	≥ 7.0%	2173	-3.87 (-4.83 to -2.90); P<0.001	-2.39 (-3.47 to -1.31); P<0.001	-2.39 (-3.47 to -1.30); P<0.001

(\*) Reference group: Hb A<sub>1c</sub><7%, N=3642

(\*\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country.

(\*\*\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country; and for physician's characteristics: main specialty, main location of clinical activities, practice setting, type of practice, practice location and number of patients with diabetes/week

## -Association of PRO with CV risk factors

PRO	CV Risk Factor(*)	N	CRUDE ANALYSIS		ADJUSTED ANALYSIS**		ADJUSTED ANALYSIS***		ADJUSTED ANALYSIS****	
			Mean difference of scales scores with respect to reference group (95% CI); P value	P value	Mean difference of scales scores with respect to reference group (95% CI); P value	P value	Mean difference of scales scores with respect to reference group (95% CI); P value	P value	Mean difference of scales scores with respect to reference group (95% CI); P value	P value
ADDQoL	Hypertension	4670	0.14 (0.02 to 0.25)	P=0.017	0.16 (0.05 to 0.27)	P=0.006	0.15 (0.03 to 0.27)	P=0.018	0.15 (0.03 to 0.27)	P=0.018
DTSQphysician	Hypertension	4670	-0.30 (-0.65 to 0.06)	P=0.106	-0.19 (-0.56 to 0.17)	P=0.292	-0.20 (-0.59 to 0.19)	P=0.310	-0.20 (-0.59 to 0.19)	P=0.309
DTSQpatient	Hypertension	4670	-0.40 (-0.80 to 0.00)	P=0.050	-0.29 (-0.69 to 0.12)	P=0.169	-0.08 (-0.52 to 0.36)	P=0.733	-0.08 (-0.52 to 0.36)	P=0.730
IIFS II	Hypertension	4670	-0.42 (-1.46 to 0.62)	P=0.434	-0.65 (-1.71 to 0.40)	P=0.227	-0.68 (-1.79 to 0.44)	P=0.234	-0.65 (-1.77 to 0.48)	P=0.259
EuroQoL	Hypertension	4670	0.47 (-0.72 to 1.67)	P=0.437	0.97 (-0.24 to 2.18)	P=0.118	1.14 (-0.15 to 2.44)	P=0.083	1.16 (-0.14 to 2.47)	P=0.080
ADDQoL	Overweight	2264	-0.07 (-0.19 to 0.06)	P=0.298	-0.09 (-0.22 to 0.04)	P=0.176	-0.07 (-0.22 to 0.08)	P=0.344	-0.07 (-0.21 to 0.08)	P=0.360
	Obese	2650	-0.21 (-0.36 to -0.11)	P<0.001	-0.28 (-0.41 to -0.15)	P<0.001	-0.23 (-0.37 to -0.08)	P=0.003	-0.23 (-0.37 to 0.08)	P=0.002
DTSQphysician	Overweight	2264	-0.13 (-0.53 to 0.28)	P=0.539	-0.13 (-0.54 to 0.28)	P=0.537	-0.01 (-0.46 to 0.44)	P=0.966	-0.02 (-0.47 to 0.44)	P=0.944
	Obese	2650	-1.01 (-1.44 to -0.64)	P<0.001	-1.05 (-1.46 to -0.64)	P<0.001	-0.60 (-1.06 to -0.14)	P=0.011	-0.61 (-1.07 to -0.15)	P=0.010
DTSQpatient	Overweight	2264	0.25 (-0.21 to 0.71)	P=0.290	0.20 (-0.27 to 0.68)	P=0.396	0.25 (-0.27 to 0.78)	P=0.347	0.25 (-0.28 to 0.78)	P=0.352
	Obese	2650	-0.62 (-1.08 to -0.16)	P=0.008	-0.65 (-1.12 to -0.18)	P=0.007	-0.45 (-0.98 to 0.08)	P=0.098	-0.46 (-1.00 to 0.07)	P=0.090
IIFS II	Overweight	2264	-0.83 (-2.04 to 0.38)	P=0.181	-0.92 (-2.15 to 0.31)	P=0.144	-1.32 (-2.66 to 0.03)	P=0.055	-1.30 (-2.65 to 0.05)	P=0.059
	Obese	2650	1.04 (-0.16 to 2.25)	P=0.089	1.04 (-0.19 to 2.27)	P=0.096	-0.46 (-1.82 to 0.91)	P=0.513	-0.43 (-1.80 to 0.94)	P=0.541
EuroQoL	Overweight	2264	-0.42 (-1.80 to 0.96)	P=0.547	-0.62 (-2.03 to 0.78)	P=0.383	-0.54 (-2.07 to 1.00)	P=0.493	-0.54 (-2.08 to 1.00)	P=0.490
	Obese	2650	4.50 ( 5.86 to 3.14)	P<0.001	4.67 ( 6.06 to 3.29)	P<0.001	4.13 ( 5.69 to 2.58)	P<0.001	4.15 ( 5.71 to 2.59)	P<0.001
ADDQoL	Hipercholesterolemia	1797	0.01 (-0.08 to 0.11)	P=0.760	0.02 (-0.08 to 0.11)	P=0.707	-0.01 (-0.12 to 0.10)	P=0.864	-0.01 (-0.12 to 0.10)	P=0.852
DTSQphysician	Hipercholesterolemia	1797	-0.22 (-0.53 to 0.08)	P=0.154	-0.18 (-0.49 to 0.12)	P=0.245	-0.28 (-0.62 to 0.07)	P=0.113	-0.28 (-0.62 to 0.07)	P=0.118
DTSQpatient	Hipercholesterolemia	1797	-0.57 (-0.92 to 0.22)	P=0.001	-0.53 (-0.87 to -0.18)	P=0.003	-0.54 (-0.94 to -0.15)	P=0.007	-0.54 (-0.94 to -0.14)	P=0.008
IIFS II	Hipercholesterolemia	1797	0.87 (-0.03 to 1.77)	P=0.057	0.82 (-0.08 to 1.72)	P=0.073	0.60 (-0.40 to 1.61)	P=0.239	0.55 (-0.46 to 1.55)	P=0.289
EuroQoL	Hipercholesterolemia	1797	-1.25 (-2.28 to -0.22)	P=0.017	-1.11 (-2.13 to -0.09)	P=0.034	-1.23 (-2.39 to -0.07)	P=0.037	-1.26 (-2.42 to -0.09)	P=0.034

(\*) Risk factors defined as: Hypertension = BP  $\geq$  130/80 mmHg (reference group BP < 130/80 mmHg, N=1145); Overweight=BMI $\geq$ 25&<30 and Obese=BMI $\geq$ 30 (reference group Normal weight BMI<25, N=901); hipercholesterolemia=total cholesterol>200mg/dl (reference group normal total cholesterol < 200 mg/dL, N=3830)

(\*\*)Adjusted for other cardiovascular risk factors: body mass index and total cholesterol

(\*\*\*)Adjusted for other cardiovascular risk factors: body mass index and total cholesterol and, other patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, and country.

(\*\*\*\*)Adjusted for other cardiovascular risk factors: body mass index and total cholesterol; other patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, and country; and for physician's characteristics: main specialty, main location of clinical activities, practice setting, type of practice, practice location and number of patients with diabetes/week.

**- Diabetes-related QoL as a function of treatment satisfaction**

	<b>CRUDE ANALYSIS</b>	<b>ADJUSTED ANALYSIS<sup>+</sup></b>	<b>ADJUSTED ANALYSIS<sup>++</sup></b>
	<b>Average change in ADD-QoL per 1 point increase in DTSQ (95% CI); P value</b>	<b>Average change in ADD-QoL per 1 point increase in DTSQ (95% CI); P value</b>	<b>Average change in ADD-QoL per 1 point increase in DTSQ (95% CI); P value</b>
<b>DTSQ physician</b>	0.06 (0.05 to 0.07); P<0.001	0.05 (0.04 to 0.05); P<0.001	0.04 (0.04 to 0.05); P<0.001
<b>DTSQ patient</b>	0.05 (0.04 to 0.06); P<0.001	0.04 (0.03 to 0.05); P<0.001	0.04 (0.03 to 0.05); P<0.001

(\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country.

(\*\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country; and for physician's characteristics: main specialty, main location of clinical activities, practice setting, type of practice, practice location and number of patients with diabetes/week

**-Changes in health resources utilization in relation to the number of hypoglycaemic episodes.**

<b>CRUDE ANALYSIS</b>	<b>ADJUSTED ANALYSIS<sup>+</sup></b>	<b>ADJUSTED ANALYSIS<sup>++</sup></b>
<b>OR of emergency department visits and/or hospitalizations per 1 point increase in n°of severe hypoglycemic episodes in the past year (95% CI); P-value</b>	<b>OR of emergency department visits and/or hospitalizations per 1 point increase in n°of severe hypoglycemic episodes in the past year (95% CI); P-value</b>	<b>OR of emergency department visits and/or hospitalizations per 1 point increase in n°of severe hypoglycemic episodes in the past year (95% CI); P-value</b>
1.14 (1.07 to 1.22); P <0.001	1.17 (1.08 to 1.26); P <0.001	1.16 (1.07 to 1.25); P <0.001

(\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country.

(\*\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country; and for physician's characteristics: main specialty, main location of clinical activities, practice setting, type of practice, practice location and number of patients with diabetes/week

## -QoL and treatment satisfaction, fear of hypoglycaemia and health status in participant countries

	Country*	N	CRUDE ANALYSIS	ADJUSTED ANALYSIS**	ADJUSTED ANALYSIS***
			Mean difference of scales scores with respect to Greece (95% CI); P value	Mean difference of scales scores with respect to Greece (95% CI); P value	Mean difference of scales score with respect to Greece (95% CI); P value
<b>ADDQoL</b>	<b>Netherlands</b>	611	1.31 ( 0.97 to 1.65); P<0.001	1.22 ( 0.87 to 1.57) ; P<0.001	0.88 ( 0.40 to 1.36); P<0.001
	<b>Belgium</b>	659	0.62 ( 0.30 to 0.94) ; P<0.001	0.72 ( 0.38 to 1.06) ; P<0.001	0.26 (-0.21 to 0.73); P=0.272
	<b>France</b>	759	0.25 (-0.06 to 0.56); P=0.114	0.32 (-0.02 to 0.66) ; P= 0.065	-0.20(-0.67 to 0.27) ; P=0.404
	<b>Spain</b>	752	0.23 (-0.09 to 0.54); P=0.156	0.29 (-0.05 to 0.62) ; P= 0.095	0.02 (-0.45 to 0.49); P=0.941
	<b>Italy</b>	752	0.33 (-0.09 to 0.76); P=0.124	0.45 ( 0.01 to 0.89) ; P= 0.043	0.40 (-0.13 to 0.94); P=0.140
	<b>UK</b>	501	0.48 ( 0.14 to 0.82); P= 0.006	0.44 ( 0.09 to 0.79) ; P= 0.013	0.21 (-0.29 to 0.71); P=0.402
	<b>Germany</b>	808	0.92 ( 0.60 to 1.24); P<0.001	1.02 ( 0.68 to 1.37); P<0.001	0.91 ( 0.49 to 1.34); P<0.001
	<b>Turkey</b>	600	-1.35 (-1.67 to -1.03); P<0.001	-1.18 (-1.52 to -0.84) ; P<0.001	-1.33(-1.77 to -0.89); P<0.001
<b>DTSQphysician</b>	<b>Netherlands</b>	611	-0.58 (-2.32 to 1.16);P=0.512	-0.68 (-2.54 to 1.19);P=0.478	-0.93 (-3.52 to 1.67);P=0.484
	<b>Belgium</b>	659	-1.06 (-2.67 to 0.54);P=0.194	-0.78 (-2.53 to 0.97);P=0.381	-1.36 (-3.86 to 1.14);P=0.286
	<b>France</b>	759	-1.96 (-3.50 to -0.42);P=0.013	-1.78 (-3.51 to -0.06);P=0.043	-2.52 (-5.00 to -0.04);P=0.047
	<b>Spain</b>	752	-0.80 (-2.38 to 0.77);P=0.317	-0.23 (-1.96 to 1.51);P=0.797	-0.47 (-3.00 to 2.06);P=0.715
	<b>Italy</b>	752	0.30 (-2.06 to 2.65);P=0.805	1.16 (-1.41 to 3.73);P=0.375	0.79 (-2.29 to 3.88);P=0.614
	<b>UK</b>	501	-1.89 (-3.60 to -0.17);P=0.031	-1.74 (-3.57 to 0.09);P=0.063	-1.76 (-4.47 to 0.96);P=0.205
	<b>Germany</b>	808	0.16 (-1.47 to 1.78);P=0.851	0.42 (-1.39 to 2.23);P=0.649	0.61 (-1.67 to 2.89);P=0.598
	<b>Turkey</b>	600	-3.47 (-5.10 to -1.84);P<0.001	-2.82 (-4.58 to -1.07);P=0.002	-3.32 (-5.67 to -0.97);P=0.006
<b>DTSQpatient</b>	<b>Netherlands</b>	611	2.68 ( 1.33 to 4.02);P<0.001	2.49 ( 1.04 to 3.93);P=0.001	1.47 (-0.55 to 3.49);P=0.155
	<b>Belgium</b>	659	1.16 (-0.10 to 2.42);P=0.070	1.33 (-0.04 to 2.71);P=0.058	0.15 (-1.82 to 2.12);P=0.882
	<b>France</b>	759	-1.45 (-2.67 to -0.24);P=0.019	-1.36 (-2.74 to 0.02);P=0.054	-2.58 (-4.57 to -0.60);P=0.011
	<b>Spain</b>	752	0.81 (-0.44 to 2.05);P=0.204	0.81 (-0.57 to 2.18);P=0.250	-0.30 (-2.30 to 1.70);P=0.770
	<b>Italy</b>	752	1.44 (-0.29 to 3.17);P=0.103	1.95 ( 0.07 to 3.83);P=0.042	0.97 (-1.38 to 3.32);P=0.417
	<b>UK</b>	501	2.88 ( 1.55 to 4.22);P<0.001	2.91 ( 1.49 to 4.33);P<0.001	1.82 (-0.30 to 3.94);P=0.093
	<b>Germany</b>	808	2.08 ( 0.82 to 3.34);P=0.001	2.66 ( 1.25 to 4.07); P<0.001	2.19 ( 0.39 to 3.98);P=0.017
	<b>Turkey</b>	600	-2.04 (-3.31 to -0.77);P<0.001	-1.74 (-3.11 to -0.37);P<0.013	-2.36 (-4.20 to -0.52);P=0.012
<b>HFS II</b>	<b>Netherlands</b>	611	-7.64 (-11.03 to -4.25);P<0.001	-6.42 (-9.84 to -3.01);P<0.001	-3.67 (-8.37 to 1.02);P= 0.125
	<b>Belgium</b>	659	-2.54 (-5.72 to 0.64);P= 0.117	-3.02 (-6.30 to 0.26);P= 0.071	-0.02 (-4.61 to 4.57);P= 0.993
	<b>France</b>	759	-0.69 (-3.78 to 2.40);P= 0.661	-1.54 (-4.85 to 1.76);P= 0.360	1.44 (-3.19 to 6.07);P= 0.543
	<b>Spain</b>	752	-3.29 (-6.44 to -0.15);P= 0.040	-3.31 (-6.58 to -0.05);P= 0.047	0.05 (-4.59 to 4.69);P= 0.982
	<b>Italy</b>	752	8.41 ( 4.03 to 12.79);P<0.001	8.11 ( 3.67 to 12.54);P<0.001	8.45 ( 3.01 to 13.88);P= 0.002
	<b>UK</b>	501	-4.68 (-8.06 to -1.31);P= 0.007	-3.60 (-6.97 to -0.23);P= 0.036	0.04 (-4.89 to 4.97);P= 0.987
	<b>Germany</b>	808	-3.26 (-6.45 to -0.08);P= 0.045	-4.67 (-7.99 to -1.34);P= 0.006	-2.71 (-6.86 to 1.44);P= 0.201
	<b>Turkey</b>	600	6.27 ( 3.07 to 9.48);P<0.001	5.56 ( 2.29 to 8.83);P= 0.001	8.81 ( 4.53 to 13.08);P<0.001
<b>EuroQoL</b>	<b>Netherlands</b>	611	0.58 (-2.84 to 4.00);P= 0.739	1.04 (-2.62 to 4.70);P= 0.578	0.22 (-4.90 to 5.35);P= 0.932
	<b>Belgium</b>	659	-5.26 (-8.47 to -2.05);P= 0.001	-1.77 (-5.27 to 1.73);P= 0.322	-2.89 (-7.90 to 2.11);P= 0.256
	<b>France</b>	759	-5.97 (-9.09 to -2.84);P<0.001	-4.12 (-7.66 to -0.58);P= 0.022	-4.96 (-10.01 to 0.09);P= 0.054
	<b>Spain</b>	752	-5.43 (-8.63 to -2.22);P= 0.001	-2.65 (-6.19 to 0.88);P= 0.141	-3.36 (-8.43 to 1.71);P= 0.194
	<b>Italy</b>	752	-1.96 (-6.17 to 2.26);P= 0.363	0.30 (-4.30 to 4.90);P= 0.897	-1.01 (-6.81 to 4.79);P= 0.733
	<b>UK</b>	501	-2.00 (-5.40 to 1.40);P= 0.250	-0.51 (-4.12 to 3.10);P= 0.783	-0.79 (-6.16 to 4.58);P= 0.773
	<b>Germany</b>	808	-4.85 (-8.05 to -1.65);P= 0.003	-2.56 (-6.12 to 1.00);P= 0.159	-2.05 (-6.57 to 2.47);P= 0.375
	<b>Turkey</b>	600	-9.41 (-12.67 to -6.15);P<0.001	-8.29 (-11.82 to -4.76);P<0.001	-9.29 (-13.97 to -4.61);P<0.001

(\*) Reference group: Greece, N=375

(\*\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country.

(\*\*\*)Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country; and for physician's characteristics: main specialty, main location of clinical activities, practice setting, type of practice, practice location and number of patients with diabetes/week

**- Physicians' perception of patients' treatment satisfaction compared with patients' treatment satisfaction**

<b>CRUDE ANALYSIS</b>	<b>ADJUSTED ANALYSIS*</b>	<b>ADJUSTED ANALYSIS**</b>
<b>Average change in DTSQ<sub>physician</sub> per 1 point increase in DTSQ<sub>patient</sub> (95% CI); P-value</b>	<b>Average change in DTSQ<sub>physician</sub> per 1 point increase in DTSQ<sub>patient</sub> (95% CI); P-value</b>	<b>Average change in DTSQ<sub>physician</sub> per 1 point increase in DTSQ<sub>patient</sub> (95% CI); P-value</b>
0.38 (0.35 to 0.40); P <0.001	0.34 (0.31 to 0.36); P <0.001	0.34 (0.31 to 0.36); P <0.001

(\*).Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country.

(\*\*).Adjusted for patient's characteristics: age, sex, age of leaving full time education, occupation, smoking status, alcohol consumption, physical activity, duration of diabetes, body mass index, systolic blood pressure, and country; and for physician's characteristics: main specialty, main location of clinical activities, practice setting, type of practice, practice location and number of patients with diabetes/week