

## Supplemental Online Content

Hansen HG, Starzer M, Nilsson SF, Hjorthøj C, Albert N, Nordentoft M. Clinical recovery and long-term association of specialized early intervention services vs treatment as usual among individuals with first-episode schizophrenia spectrum disorder: 20-year follow-up of the OPUS trial. *JAMA Psychiatry*. Published online February 22, 2023. doi:10.1001/jamapsychiatry.2022.5164

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This supplemental material has been provided by the authors to give readers additional information about their work.

<b>eTable 1. Baseline characteristics among participants and non-participants at 20-year follow-up</b>				
	All, n=547	Participants, n=164	Non-participants, n=383	P value
<i>Sociodemographics, n (%)</i>				
Age, mean (SD)	26.6 (6.4)	25.5 (5.6)	27.1 (6.6)	<b>.007</b>
Sex, Female,	224 (41.0)	85 (51.8)	139 (36.3)	<b>.001</b>
Studying or working	142 (26.4)	53 (32.7)	89 (23.7)	<b>.03</b>
Completed high school	181 (33.6)	68 (41.5)	113 (30.2)	<b>.01</b>
In a relationship	133 (24.7)	43 (26.4)	90 (23.9)	.55
Being a parent	79 (14.6)	19 (11.7)	60 (15.9)	.20
<i>Premorbid functioning, mean (SD)</i>				
Premorbid social functioning <sup>1</sup>	0.27 (0.22)	0.26 (0.22)	0.28 (0.22)	.59
Premorbid academic functioning <sup>2</sup>	0.38 (0.21)	0.35 (0.20)	0.39 (0.21)	.06
<i>Living conditions, n (%)</i>				
Living alone	332 (61.7)	106 (65.4)	226 (60.1)	.68
Living with children	16 (3.0)	5 (3.1)	11 (2.9)	
Living with a partner	73 (13.6)	23 (14.2)	50 (13.3)	
Living with parents	90 (16.7)	23 (14.2)	67 (17.8)	
Living in supported housing	3 (0.6)	0 (0.0)	3 (0.8)	
Homelessness	24 (4.5)	5 (3.1)	19 (5.1)	
Independent living	421 (78.3)	134 (82.7)	287 (76.3)	.10
<i>Symptom dimension, mean (SD)</i>				
Psychotic dimension <sup>3</sup> (excl. F21)	2.96 (1.31)	3.00 (1.37)	2.94 (1.28)	.63
Negative dimension <sup>4</sup>	2.15 (1.15)	1.93 (1.12)	2.25 (1.16)	<b>.003</b>
Disorganized dimension <sup>5</sup>	1.02 (0.95)	0.88 (0.90)	1.07 (0.96)	<b>.04</b>
<i>Global functioning score, mean (SD)</i>				
GAF-F <sup>6</sup> , Function scale	41.32 (13.34)	44.52 (13.20)	39.93 (13.18)	<b>.000</b>
GAF-S <sup>7</sup> , Symptom scale	33.53 (10.68)	34.98 (10.53)	32.89 (10.70)	<b>.04</b>
<i>Antipsychotic treatment (at one year follow-up), n (%)</i>				
Antipsychotic use	334 (61.1)	98 (59.8)	236 (61.6)	.68
<i>Diagnoses, n (%)</i>				
Alcohol/substance use disorder	146 (26.7)	40 (24.4)	106 (27.7)	.43
Schizophrenia (F20)	362 (66.2)	104 (63.4)	258 (67.4)	.24
Schizotypal disorder (F21)	79 (14.4)	30 (18.3)	49 (12.8)	.24
Others (F22-F29)	106 (19.4)	30 (18.3)	76 (19.8)	.24
<i>Duration of untreated psychosis (DUP in weeks), median (range)<sup>8</sup></i>				
DUP, weeks, (excl. F21)	48.0 (0-1248)	52.8 (0-848)	43.0 (0-1248)	.60

<sup>1</sup> Premorbid Adjustment Scale (Premorbid social functioning)<sup>44</sup>

<sup>2</sup> Premorbid Adjustment Scale (Premorbid academic functioning)<sup>44</sup>

<sup>3</sup> Scale for Assessment for Positive Symptoms (SAPS)<sup>21</sup>

<sup>4</sup> Scale for Assessment of Negative Symptoms (SANS)<sup>22</sup>

<sup>5</sup> Disorganized symptoms were assessed using SANS and SAPS

<sup>6</sup> Global Assessment of Functioning scale<sup>23</sup>

<sup>7</sup> GAF-S

<sup>8</sup> Duration of Untreated Psychosis (DUP)<sup>45</sup>

**eTable 2. Baseline characteristics among participants and non-participants at 20-year follow-up divided between the OPUS-group and TAU-group**

	All, n=547	OPUS Participant s, n=84	OPUS, Non- participants, n=191	P value	TAU Participants, n=80	TAU, Non- participants, n=192	P value
<i>Sociodemographics, n (%)</i>							
Age, mean (SD)	26.6 (6.4)	26.65 (5.8)	26.69 (6.6)	.97	24.29 (5.2)	27.51 (6.6)	<b>.000</b>
Sex, Female,	224 (41.0)	47 (56.0)	69 (36.1)	<b>.002</b>	38 (47.5)	70 (36.5)	.09
Studying or working	142 (26.4)	25 (30.1)	50 (26.5)	.53	28 (35.4)	39 (20.9)	<b>.01</b>
Completed high school	181 (33.6)	33 (39.3)	65 (34.2)	.42	35 (43.8)	48 (26.1)	<b>.004</b>
In a relationship	133 (24.7)	20 (24.1)	37 (19.6)	.40	23 (28.8)	53 (28.3)	.95
Being a parent	79 (14.6)	14 (16.9)	28 (14.7)	.65	5 (6.3)	32 (17.1)	<b>.02</b>
<i>Living conditions, n (%)</i>							
Living alone	332 (61.7)	52 (63.4)	113 (59.5)	.20	54 (67.5)	113 (60.8)	.48
Living with children	16 (3.0)	5 (6.1)	5 (2.6)		0 (0.0)	6 (3.2)	
Living with a partner	73 (13.6)	12 (14.6)	21 (11.1)		11 (13.8)	29 (15.6)	
Living with parents	90 (16.7)	12 (14.6)	37 (19.5)		11 (13.8)	30 (16.1)	
Living in supported housing	3 (0.6)	0 (0.0)	1 (0.5)		0 (0.0)	2 (1.1)	
Homelessness	24 (4.5)	1 (1.2)	13 (6.8)		5 (2.7)	4 (5.0)	
Independent living	421 (78.3)	69 (84.1)	139 (73.2)	<b>.05</b>	65 (81.3)	148 (78.6)	.753
<i>Symptom dimension, mean (SD)</i>							
Psychotic dimension <sup>3</sup> (excl. F21)	2.96 (1.31)	3.14 (1.42)	3.12 (1.25)	0.90	2.88 (1.33)	2.76 (1.29)	.50
Negative dimension <sup>4</sup>	2.15 (1.15)	2.02 (1.15)	2.22 (1.14)	.20	1.84 (1.08)	2.29 (1.18)	<b>.004</b>
Disorganized dimension <sup>5</sup>	1.02 (0.95)	0.93 (0.91)	1.09 (0.95)	.22	0.83 (0.90)	1.06 (0.97)	.08
<i>Global functioning score, mean (SD)</i>							
GAF-F <sup>6</sup> , Function scale	41.32 (13.34)	45.14 (13.05)	40.08 (12.85)	<b>.003</b>	43.86 (13.41)	39.77 (13.53)	<b>.02</b>
GAF-S <sup>7</sup> , Symptom scale	33.53 (10.68)	35.41 (10.75)	31.45 (9.91)	<b>.003</b>	34.54 (10.34)	34.36 (11.28)	.90
<i>Antipsychotic treatment (at one year follow-up), n (%)</i>							
Antipsychotic use	334 (61.1)	55 (65.5)	127 (66.5)	.87	43 (53.8)	109 (56.8)	.65
<i>Diagnoses, n (%)</i>							
Alcohol/substance use disorder	146 (26.7)						
Schizophrenia (F20)	362 (66.2)	52 (61.9)	133 (69.6)		52 (65.0)	125 (65.1)	
Schizotypal disorder (F21)	79 (14.4)	19 (22.6)	22 (12.0)	<b>.03</b>	11 (13.8)	26 (13.5)	.96
Others (F22-F29)	106 (19.4)	13 ( )	35 ( )		17 ( )	41 ( )	
<i>Duration of untreated psychosis (DUP), median (range)<sup>8</sup></i>							
DUP, weeks, (excl. F21)	48.0 (0-1248)	52.9 (0-832)	39.0 (0-1248)	.56	52.29 (0-848)	51.9 (0-970)	.85

<sup>3</sup> Scale for Assessment for Positive Symptoms (SAPS)<sup>21</sup>

<sup>4</sup> Scale for Assessment of Negative Symptoms (SANS)<sup>22</sup>

<sup>5</sup> Disorganized symptoms were assessed using SANS and SAPS

<sup>6</sup> Global Assessment of Functioning scale<sup>23</sup>

<sup>7</sup> GAF-S

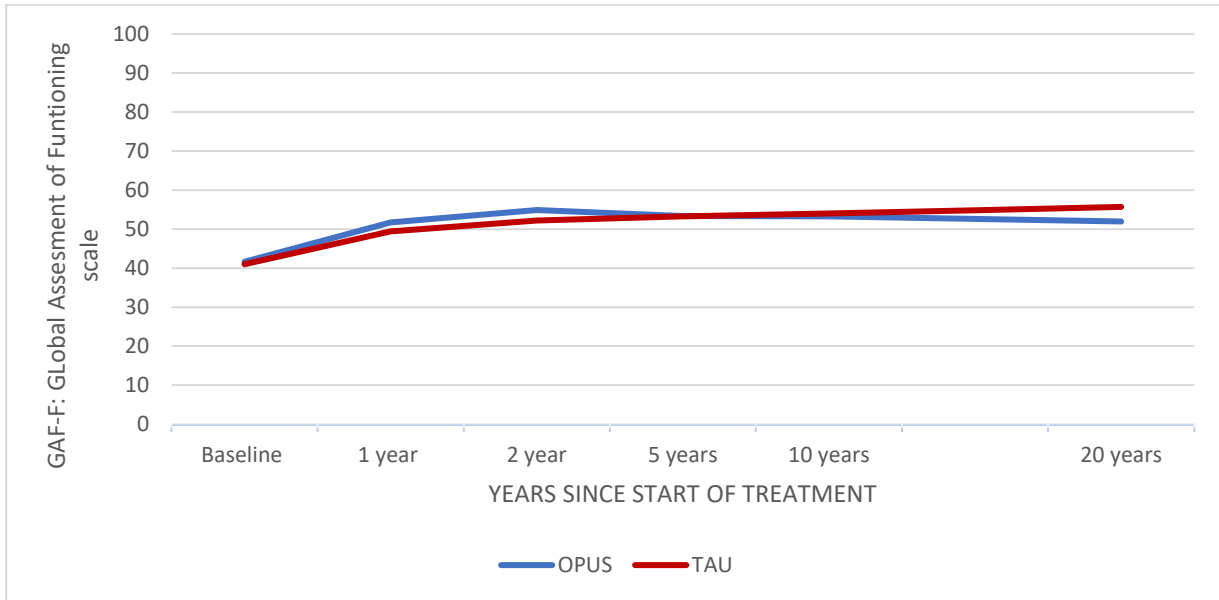
<sup>8</sup> Duration of Untreated Psychosis (DUP)<sup>45</sup>

<b>eTable 3. Last observation characteristics (excluding the 20-year assessment) among participants and non-participants at 20-year follow-up divided between the OPUS-group and TAU-group</b>							
	All, n=547	OPUS Participant s, n=84	OPUS, Non- participants, n=191	P value	TAU Participants, n=80	TAU, Non- participants, n=192	P value
<i>Symptom dimension, mean (SD)</i>							
Psychotic dimension <sup>3</sup> (excl. F21)	1.38 (1.52)	1.02 (1.45)	1.51 (1.49)	<b>0.03</b>	0.93 (1.38)	1.58 (1.57)	<b>0.004</b>
Negative dimension <sup>4</sup>	1.73 (1.22)	1.33 (1.09)	1.88 (1.16)	<b>&lt;0.001</b>	1.26 (1.03)	1.95 (1.33)	<b>&lt;0.001</b>
Disorganized dimension <sup>5</sup>	0.57 (0.76)	0.40 (0.62)	0.64 (0.82)	<b>0.02</b>	0.44 (0.66)	0.63 (0.78)	0.06
GAF-F <sup>6</sup> , Function scale	52.16 (16.53)	60.15 (16.67)	49.21 (15.26)	<b>&lt;0.001</b>	57.98 (15.11)	49.16 (16.58)	<b>&lt;0.001</b>
GAF-S <sup>7</sup> , Symptom scale	51.21 (16.72)	57.77 (16.75)	48.53 (15.68)	<b>&lt;0.001</b>	56.19 (16.13)	48.94 (16.84)	<b>0.001</b>

**eTable 4: Psychiatric Hospitalizations and Outpatient Contacts at one-two, two-five, five-ten and ten-20 Years after Randomization into Early Intervention Services (OPUS-treatment) vs. TAU**

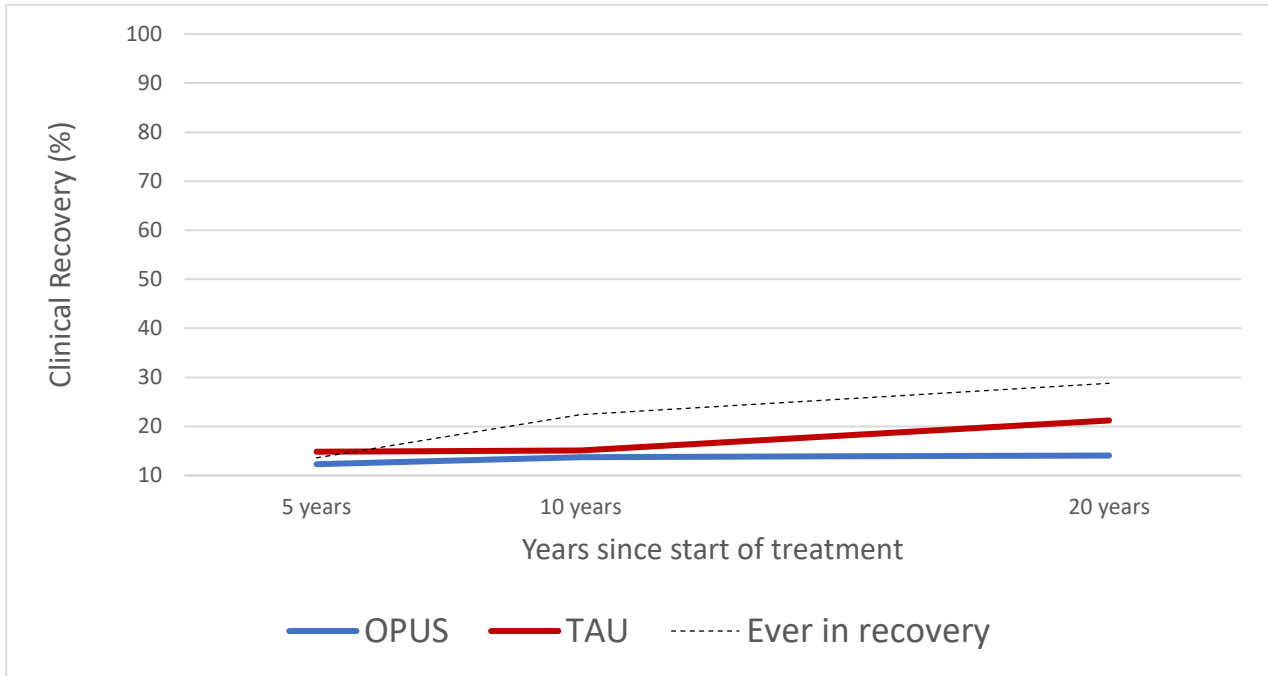
	OPUS mean (SE)	TAU mean (SE)	Incidence Rate Ratio (95% CI)	P Value
Psychiatric hospitalizations (mean days/year)				
0-2 y after randomization	46.78 (4.397)	60.87 (5.047)	0.768 (0.601; 0.983)	<b>.04</b>
2-5 y after randomization	19.85 (3.071)	23.90 (3.131)	0.831 (0.559; 1.234)	.36
5-10 y after randomization	15.06 (2.758)	15.48 (2.686)	0.973 (0.594; 1.594)	.91
10-20 y after randomization	11.95 (2.050)	9.93 (1.848)	1.204 (0.733; 1.977)	.46
Outpatient contacts (number of contacts/year)				
0-2 y after randomization	29.45 (1.298)	16.95 (1.223)	1.738 (1.473; 2.051)	<b>.000</b>
2-5 y after randomization	12.37 (0.881)	10.37 (0.816)	1.193 (0.969; 1.469)	.10
5-10 y after randomization	8.06 (0.718)	8.11 (0.772)	0.994 (0.769; 1.284)	.96
10-20 y after randomization	5.98 (0.679)	4.99 (0.503)	1.197 (0.889; 1.612)	.24

**eFigure 1: Global functional levels between the OPUS-group and the TAU-group since start of treatment**



<sup>1</sup> Global assessment of functioning scale<sup>24</sup> (scale from 0-100)

**eFigure 2: Percentages of Participants in Clinical Recovery at Five-, Ten- and 20-years of Follow-up**



\*Percentages based on participants at each respective follow-up

Clinical recovery: defined as no psychotic episode, no psychiatric hospitalizations and no supported accommodation for two consecutive years before follow-up and currently studying or working and a GAF-F score of  $\geq 60$ .<sup>5</sup>

**eFigure 3: Psychiatric hospitalizations and outpatient contacts between the OPUS-group and the TAU-group since start of treatment**

