

**Investigating duration of illness and duration of untreated illness in Obsessive Compulsive Disorder reveals patients remain at length pharmacologically untreated**

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975 words

18 references

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Obsessive Compulsive Disorder is a disabling condition, often associated with early onset and chronic course (Dell'Osso et al., 2013). Patients with OCD can also exhibit high degrees of comorbidity with other psychiatric disorders and increased suicidality (Dell'Osso et al., 2017; Lochner et al., 2014). A recent International multicenter investigation confirmed OCD patients can show first symptoms before adult age, with the majority of them showing childhood or adolescent onset (Dell'Osso et al., 2016). Early onset combined to the secretiveness that frequently characterizes the condition, as well as patient's beliefs that OC symptoms do not represent a medical condition and that OCD can remit spontaneously, are all factors contributing to delayed diagnosis and first treatment, particularly of pharmacological nature (Benatti et al., 2016; Dell'Osso & Altamura, 2010; Poyraz et al., 2015).

Given that age at onset and age of first pharmacological treatment concur to define the duration of untreated illness – practically computed by subtracting age at onset of a specific disorder from age of first pharmacological treatment and defined as the period of time elapsing from the onset of the disorder and the initiation of the first pharmacological treatment in therapy adherent patients, according to guidelines recommendations (Dell'Osso et al., 2013) , it is not surprising, based on the above, to observe that patients with OCD remain pharmacologically untreated for many years. Actually, published studies in the field showed that DUI in OCD can range from 3 to 8 years (Altamura et al., 2010; Bernardo Dell'Osso et al., 2013; Poyraz et al., 2015; Viswanath et al., 2011), with relevant consequences in terms of outcome and costs for affected patients, caregivers and society. While a uniform consensus on how to categorically differentiate short vs long DUI in OCD is lacking, with some studies using a threshold of 2 years and others of 4 years (Albert et al., n.d.; Poyraz et al., 2015; Vigne et al., 2018) it is noteworthy to highlight that DUI in OCD patients was found to account for at least half of the overall duration of illness (DI) in studies assessing both

variables. Over the last years, in fact, at least 5 independent studies conducted in different countries demonstrated that the largest part of the DI in OCD patients was represented by the DUI (see Table 1), meaning that assessed patients had spent the majority of their illness without receiving any pharmacological treatment.

A first Indian study comparing patients with familial vs sporadic OCD in an overall sample of 164 individuals, reported DUI values of 61.3 and 34 months, respectively, along with DI values of 95 and 69.3 months (Viswanath et al., 2011).

Subsequently, an Italian study conducted by our group on a sample of 114 patients with OCD, aimed at exploring clinical differences across different phenotypes, found respectively a mean DUI of 87.3 months and a mean DI of 172.2 months for the whole sample (Dell'Osso et al., 2014). The sample was subsequently enlarged to 124 patients divided in two groups on the basis of the severity of illness, indicating DUI and DI values of respectively 87.5 and 194.7 months (Dell'Osso et al., 2017).

In the same year, a Turkish study exploring differences between patients with a DUI below and above 4 years in an overall sample of 96 patients, reported values of DUI and DI of 7 and 12.7 years, respectively (Poyraz et al., 2015).

More recently, a Brazilian study exploring differences in patients with OCD, panic disorder and social anxiety disorder, found a DUI of 7.7 years and a DI of 19.3 years in the subsample of 30 patients suffering from OCD (Vigne et al., 2018).

Finally, a recently published Italian report on 251 patients with OCD, exploring treatment response on the basis of long vs short DUI, found a DUI of 106.2 months and a DI of 183.9 months (Albert et al., in press).

All reviewed reports, in spite of being conducted from independent groups on different samples in distinct countries, clearly converge in delineating a DUI of several years (around 7 years in the majority of them), which represented, on average, a portion ranging between the

40 and the 70% of the overall DI (see Figure 1). While it may be contended that: 1) current age of assessed samples was a major factor determining current duration of illness, implying that a higher DI/DUI ratio was easier to find in young-adult to mid-adult samples (compared to senior patients with a much longer DI), 2) that fluctuant versus chronic course is supposed to determine a different DI, and 3) that pharmacological treatment does not represent the only guideline-recommended intervention to treat OCD patients, we still contend that mean current age in the above-mentioned studies ranged from 30 to 40 years, with age at onset around 20 years, on average, which undoubtedly represent a crucial period for patients in terms of familial and work functioning.

If, on one hand, some preliminary investigation, including patients with OCD, has recently shown that DUI can also depend on the epoch of onset, with patients with more distant onset having longer DUI compared to individuals with more recent onset (Dell'Osso et al., 2016), recent morphometric imaging investigation with the largest sample of adult and pediatric OCD patients assessed to date revealed that patients compared to controls had lower cortical thickness (Boedhoe et al., 2018). This finding, along with well-established alterations documented at the level of cortico-striato-thalamo-cortical circuits in OCD, allows to hypothesize that OCD, particularly when not effectively treated, can progress and entail cerebral alterations of either structural and functional nature, along with other negative clinical and psychosocial outcomes.

Based on available literature in the field of DUI revealing that adult OCD patients had spent more than half of their illness pharmacologically untreated, we believe that mental health professionals and policy makers should focus their effort on conducting and encouraging further investigation on the epidemiologic and clinical correlates of DUI in OCD, in order to promote early diagnosis and intervention programs for affected patients (Fineberg et al., submitted).



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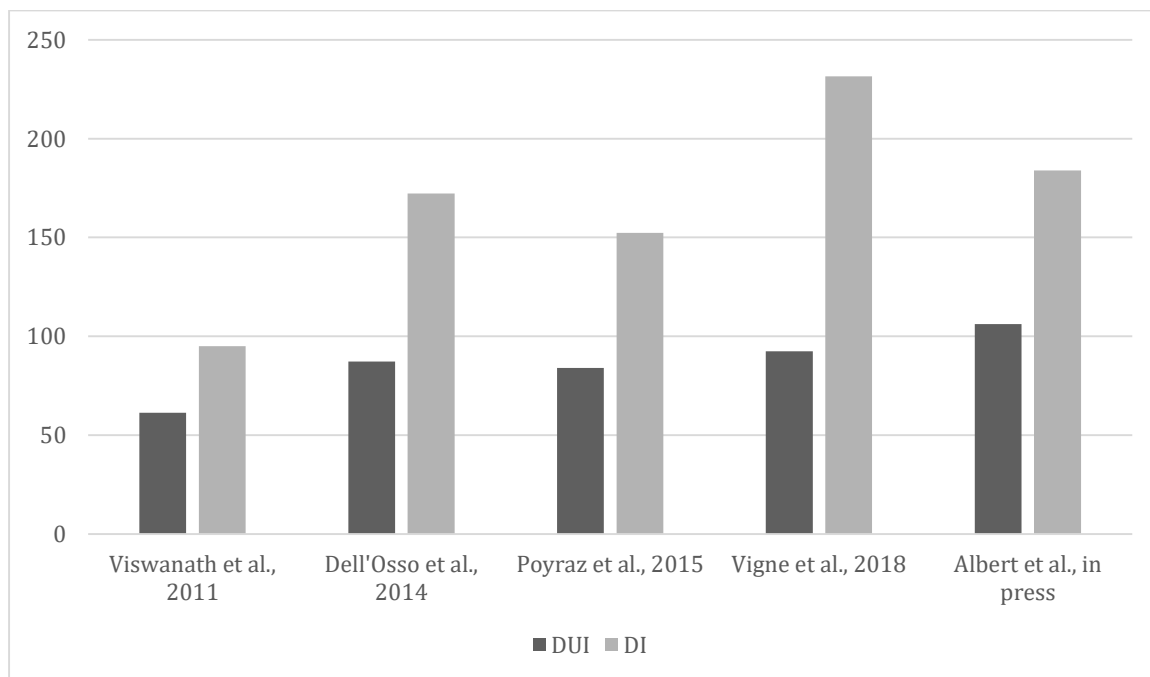


Table 1. Summary of the main features of the selcted manuscripts.

	N	Mean DUI	Mean DI
Viswanath et al., 2011	84	61.3 months/ familial OCD	95 months/ familial OCD
	80	34 months/ sporadic OCD	69.3 months/ sporadic OCD
Dell'Osso et al., 2014	114	87.3 months	172.2 months
Poyraz et al., 2015	96	84 months	152.4 months
Vigne et al., 2018	30	92.4 months	231.6 months
Albert et al, in press	251	106.2 months	183.9 months

Legend: DUI: duration of untreated illness; DI: duration of illness

Figure 1. Mean DUI and DI reported in the selected manuscripts.



Legend: DUI: duration of untreated illness; DI: duration of illness