



Title: Uremic Restless Legs Syndrome Pleads “Not Guilty”.

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## **Title Page**

**Title:** Uremic Restless Legs Syndrome pleads “not guilty”

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**Running Head:** Uremic RLS and mortality

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## Main Text:

Disorders of the brain are becoming more prevalent over time and are threatening not only the quality of life of millions of citizens but are also creating major challenges for the national health systems. Restless Legs Syndrome (RLS) (or Willis/Ekbom Disease) is one of the most common neurological disorders inducing significant personal, social and economic burden. With an adult prevalence of around 2.7% in the general population, RLS is underdiagnosed [1], estimated to be affecting 20 million of European citizens. Recent data from the “Value of treatment for brain disorders” research project, conducted by the European Brain Council\*, showed that RLS is the fifth more expensive neurological disorder after mood disorders and dementia.

Notably, RLS prevalence in hemodialysis (HD) patients is much higher than in the general population reaching approximately 30% [2, 3]. Uremic RLS has been frequently associated with increased morbidity and enhanced mortality in HD patients, linked to cardiovascular diseases [4]. A recent 3-year mortality study showed for the first time that the diagnosis of RLS according to the essential criteria of the International RLS Study Group does not seem to influence mortality in HD patients [5]. Mortality rate was 15.6% (5.2%/yr) in RLS-HD patients and 22.3% (7.4%/yr) in non-RLS HD patients with no significant association between RLS and 3-year mortality, either with age and gender as covariates. In this current issue, an unprecedented 15-year follow-up RLS survival study is presented by Baiardi et al [REF] showing that RLS-HD patients presented a lower mortality rate compared to those HD patients without the syndrome [63.8% (4.3%/yr) RLS-HD vs 87.6% (5.8%/yr) non-RLS HD,  $p = 0.04$ ]. Similarly, the mortality rate was not influenced by gender ( $p = 0.15$ ) and even more importantly, by RLS severity ( $p = 0.11$ ). In addition, the study by Baiardi et al, [REF] showed no difference among the causes of death between the two groups in contrast to studies linking RLS to cardiovascular diseases [4]. The studies by Stefanidis et al [5] and by Baiardi et al, [REF] clearly suggest that mortality in HD patients is not influenced by the presence of RLS/WED, with no clinical evidence linking uremic RLS/WED and cardiovascular mortality. Considering the discordant literature results on the mortality risk in uremic RLS patients, and the fact that cardiovascular disease is the number one cause of death in HD patients, the recent evidence by Baiardi et al, [REF] will help design the next prospective studies to address other possibly non-traditional uremia-related variables for reducing cardiovascular mortality and to improve patients' survival and quality of life. RLS symptoms during HD sessions and during rest hours continue to be one of the most disturbing disease factors for HD patients. RLS impacts on affecting patients' quality of life and their overall health mainly by increasing depressive symptoms. Unfortunately, due to limited knowledge of the disease and possible treatment, patients often go through long periods of suffering until the correct diagnosis is made and proper treatment started. This leads to an unnecessary burden on health care budgets and severely deterioration of patients' mood status. Extensive education of both patients and nephrologists is needed to improve this situation. Since at the moment there is no cure and the existing available treatments are far from optimal,

more research into the pathophysiology of uremic RLS and its disease mechanism is needed to provide specific symptomatic and future curative treatments.

## References

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- \* [www.braincouncil.eu/activities/news/press-release-value-of-treatment-for-brain-disorders-in-europe/](http://www.braincouncil.eu/activities/news/press-release-value-of-treatment-for-brain-disorders-in-europe/)