Patient Insight:
Patient journey reveals cost of Restless Legs Syndrome (RLS)

Abstract

Objective: The objective of the study was to quantify RLS misdiagnosis and delayed treatment in primary care and to examine the implications for the RLS patient journey and associated healthcare costs.

Background: Restless legs syndrome (RLS) affects around 5-10% of adults in Western countries. However, awareness of the disease is relatively low: around 2 in 5 people in the UK have heard of it. Low awareness may be one reason it is misdiagnosed or diagnosed late. Late diagnosis and misdiagnosis has implications for the cost of the disorder to the health service.

Method: An online questionnaire-based study of 157 adult patients with RLS from the UK was conducted in 2012.

Results: The survey found it took an average of 7.53 visits for participants to receive an RLS diagnosis with some stating it took 20, 30 or more visits before a diagnosis was reached. For the majority (67%) it had taken over a year to be diagnosed with RLS. However, 23% of this group of respondents noted it had taken 10 years or more before they were diagnosed.

Of the 15% of the study population who had indicated that their treatment had been changed, almost half (46%) had had one change made to their treatment; 21% had had three changes made, and one respondent claimed to have had 13 changes made.

Half of respondents (50%) said pain was affecting their daily life or quality of life: 21% indicated that pain was ‘very severely’ affecting their quality of life and daily life.

Discussion: Data on the time it took to obtain a diagnosis and the number of changes in therapy suggest a significant level of delayed diagnosis and misdiagnosis. Based on the average number of visits before a diagnosis was obtained there was a potential cost of between £489.75 and £714.75 per misdiagnosed patient taking into account visits to specialists. That compares with the cost of £25 for a first-time diagnosis by a GP.
Introduction

The objective of the study was to quantify RLS misdiagnosis and delayed treatment in primary care and to examine the implications for the RLS patient journey and associated healthcare costs.

Restless legs syndrome (RLS), or Willis-Ekbom disease, is not generally a well known condition, figures suggest only 2 in 5 people in the UK have heard of the disorder.¹

RLS is a neurological condition typically characterised by an irresistible urge to move the legs in an attempt to stop or ease uncomfortable and odd sensations.² Symptoms occur primarily when a person is relaxing or at rest and can increase in severity at night. Often called paresthesias (abnormal sensations) or dysesthesias (unpleasant abnormal sensations), the sensations range from uncomfortable to irritating to painful.³ Most people with RLS have difficulty sleeping. Left untreated, the condition can lead to exhaustion and daytime fatigue.³

Even though RLS may not be widely recognised, it is relatively common, affecting 5-10% of adults in Western countries. Several studies have shown that moderate-to-severe RLS affects approximately 2-3% of adults. An additional 5% appear to be affected by a milder form.⁴ Symptoms may begin at any age although prevalence is higher in older age,⁵ with women twice as likely to develop RLS than men.⁶

RLS is often misdiagnosed or diagnosed late.⁷ Some people with symptoms of RLS will not seek medical attention, believing they will not be taken seriously, that their symptoms are too mild, or that their condition is untreatable.⁸

RLS is generally a lifelong condition for which there is no cure. Nevertheless, current therapies can control symptoms thus increasing periods of restful sleep. Some individuals

¹ ICM survey data. Conducted Feb 2012.
³ http://www.ninds.nih.gov/disorders/restless_legs/detail_restless_legs.htm
⁴ www.ninds.nih.gov
⁵ Zucconi M, Ferini-Strambi L. EPIDEMIOLOGY AND CLINICAL FINDINGS OF RESTLESS LEGS SYNDROME
⁶ NHS Choices Website: Restless Legs Syndrome
⁹ www.ninds.nih.gov
have remissions – periods in which symptoms decrease or disappear for days, weeks, or months – although symptoms usually eventually reappear.\(^9\)

Revised European guidelines on management of RLS published in 2012\(^{10}\) highlight the importance of understanding the complete patient journey.

RLS is possibly one of the more manageable medical causes of insomnia, so it is important that healthcare professionals are familiar with the disorder.\(^{11}\) Investigation of the RLS patient journey should give healthcare professionals a better understanding and knowledge of the condition which, in turn, should result in more accurate, earlier diagnosis and more effective treatment. Furthermore, the positive implications of this will benefit governmental health expenditure.

**Methodology**

An online questionnaire-based study was conducted in 2012 among adult UK patients who had been physician-diagnosed with RLS.

Patient Intelligence Panel (PIP Health) developed the questionnaire, in collaboration with this paper’s authors. PIP Health implements patient insight research through its patient panel which secured the study sample, programmed the questionnaire and performed the online fieldwork. The sampling plan was designed to generate a study population representative, in terms of age and gender, of the population of patients in the UK living with diagnosed RLS.

Potential study participants were invited by email to participate in an internet survey which would take approximately 10 minutes to complete and offered a GBP £1 donation to the RLS UK charity, or a charity of their choice.

The survey was designed in accordance with the Association of the British Pharmaceutical Industry (ABPI), Market Research (MRS) and British Healthcare Business Intelligence Association (BHBIA) codes of conduct regarding patient anonymity and confidentiality.

A total of 157 patients completed the questionnaire.

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9 ([www.ninds.nih.gov](http://www.ninds.nih.gov))
Parameters measured

**Symptoms**
Survey participants were asked to identify which symptoms they felt drove their RLS diagnosis. In answer to the question: 'Which of the following symptoms did you feel drove your diagnosis', participants were asked to complete the statement: ‘Irresistible and often unpleasant urge to move legs that...’ with 1 or more of the following 4 options: 'begins or worsens during rest or inactivity', 'is partially or totally relieved by movement', 'is worse in the evening or at night' or 'none of the above'.

**Time to Diagnosis - Visits to GP/other specialists**
Participants were asked to indicate when they had first experienced symptoms. They were then asked how long after first experiencing symptoms their condition had become troublesome enough to seek medical attention. Participants were then asked whether they had been diagnosed with RLS at their initial visit to a healthcare professional.

Participants not diagnosed at their initial visit were asked how many subsequent visits it had taken before receiving a RLS diagnosis and time it had taken from first developing symptoms to receiving a diagnosis.

**Treatments**
Patients were asked to identify the specific treatments they had received after diagnosis.

To examine the possible misdiagnosis of RLS participants were asked if a blood test was taken or if they were referred for a blood test at the time of diagnosis. Those who answered 'yes' were then asked to indicate the result by selecting one or more of three answers: ‘received or changed treatment/prescription’, ‘referred to another healthcare professional’, or ‘advice given, eg lifestyle changes’.

Participants were further questioned about the number of changes to their treatment since their initial treatment at diagnosis and over what time period this had happened.

**Quality of life/pain /changes to symptoms (positive/negative)**
To investigate how symptoms had changed since diagnosis respondents were asked about the three most common symptoms of RLS: ‘sleep disturbance’; ‘urge to move the legs’, and ‘uncomfortable/unpleasant sensations in the legs’. They were then asked to grade the severity of symptoms on a Likert scale of -3 (significant negative change) to 3 (significant positive change) for each of the three symptoms to allow for an exploration of the effects of their RLS treatment.

Participants were also asked to indicate to what extent pain affected them.
Results

More females than males participated (79% vs. 21%, respectively) and the most common age group was 46-55 years old with a minimum age range of 18-25 years and maximum age range of 75 years or above.

Symptoms

The most frequently recognised symptom of RLS is an ‘urge to move the legs, usually accompanied by uncomfortable/unpleasant sensations in the legs’, that ‘begins or worsens during rest or inactivity’, ‘is partially or totally relieved by movement’ and ‘is worse in the evening or at night’.  

The majority (90%) confirmed ‘worse in the evening or at night’ to be the most frequently selected symptom participants believe drove their RLS diagnosis, 69% choose ‘begin or worsen during rest or inactivity’ and 41% said ‘partially or totally relieved by movement’ was to be attributed to one of the drivers to being diagnosed with RLS (Figure 1).

Figure 1. Which symptoms drove diagnosis of RLS. “irresistible and often unpleasant urge to move the legs that; ........”

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**Time to diagnosis – visits to GP/other specialists**

More than half of participating patients (52%) had been diagnosed with RLS for over 6 years and only 6% of those taking part had suffered from RLS symptoms for less than a year. Some 56% had waited for more than one year to seek medical attention for their RLS symptoms while 44% had sought medical attention within one year of experiencing symptoms (see Figure 2). Half (50%) of this group said they had seen a healthcare professional (mostly their GP) within 2 months as a result of troublesome symptoms. In contrast, 16% had waited longer than 5 years before seeking medical attention.

**Figure 2. How Long after RLS symptoms began before medical attention was sought.**

A total of 42% of respondents said they were not diagnosed at their initial visit to a healthcare professional: it took an average of 7.53 visits for those participants to receive an RLS diagnosis with some stating it took 20, 30 or more visits before a diagnosis was reached (Figure 3). Excluding these extremes, the average number of visits for an RLS diagnosis was 3.59.
Figure 3. After initial visit, how many subsequent visits were made before an RLS diagnosis was reached.

For the majority (67%) it had taken over a year to be diagnosed with RLS. However, 23% of this group of respondents noted it had taken 10 years or more before they were diagnosed.

Following diagnosis, 86% of respondents said they had not been referred to another healthcare professional and had continued their treatment with the healthcare professional that had made the diagnosis. However, 14% of respondents had been referred to another healthcare professional after diagnosis.

Treatments
Almost 9 out of 10 (89%) of survey participants were using treatment for their RLS diagnosis at the time of the study. The most common were: sleeping aids; antidepressants; mirapexin; adartel / neurotin; anticonvulsants, and iron sulphate /levodopa/carbazepine /sinemet.

A quarter of all respondents (25%) said at the time of RLS diagnosis a blood test was taken or they were referred for a blood test. The group was asked about the outcome: they were given three options and could select one or more answers: 53% noted they had ‘received or changed treatment/prescription’; 50% had ‘advice given, eg lifestyle changes’, and 23% had been ‘referred to another healthcare professional’.

Of the 15% of the study population who had indicated that their treatment had been changed, almost half (46%) had had one change made to their treatment, 21% of the group had 3 changes made to their treatment and one respondent claimed to have had 13 changes made to the treatment of their RLS.
Quality of life/pain/changes in symptoms (positive/negative)

When examining changes in the symptoms experienced by the sufferers the most common answer selected on the Likert Scale was 0 (no change) for each of the three symptoms, ‘sleep disturbance’ (32%), ‘urge to move legs’ (31%) and ‘uncomfortable/unpleasant sensations in the legs’ (32%).

However, 31% of respondents said there had been a positive change to their ‘sleep disturbance’ symptoms with only 10% of the group stating there had been a ‘significant’ positive change. In contrast, 37% experienced a negative change in ‘sleep disturbance’ symptoms and 20% said they had experienced ‘significant’ negative changes, indicating deterioration in their condition.

Similar results were seen in the other two symptom categories.

Participants were asked to identify the extent to which pain affected their daily life (see Table 1).

Table 1: Impact of pain on daily life

<table>
<thead>
<tr>
<th>Degree to which quality of life affected</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – not affected</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>29</td>
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<td>4</td>
<td>26</td>
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<td>5</td>
<td>30</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>7 – very severely affected</td>
<td>32</td>
</tr>
</tbody>
</table>
Discussion

The RLS patient journey begins when symptoms are first experienced. However, this can be difficult to pinpoint exactly. As mentioned earlier, RLS is not a generally well recognised condition in the UK, so patients may not be aware of symptoms starting.

The study found the most common symptom experienced by participants on the RLS patient journey was that the effects of the condition were worse in the evening or at night, with 90% of respondents experiencing this and identifying this aspect as the main driver for the diagnosis. This was reported as one of the main consequences of RLS in a study by the Sleep Research Institute in Spain, which found difficulties resting and remaining still happened predominantly in the evening and at night. As Garcia-Borreguero et al state in their paper: ‘Algorithms for the diagnosis and treatment of restless legs syndrome in primary care’, it can be difficult for sufferers to realise they are experiencing symptoms of RLS. Until recently RLS was considered a rare disorder; poor recognition of symptoms, the absence of symptoms during most of the day (with an onset only at night), accompanied by an often ‘bizarre’ description of symptoms, frequently led to the consideration of a psychogenic origin for these symptoms.

This lack of knowledge about the condition can lead to difficulties when trying to identify exactly when a patient first started experiencing the symptoms of RLS. The study found that the majority (52%) of those who took part were able to identify that in their opinion they had started experiencing symptoms in the last 6 years. However, and perhaps more importantly, 35% of respondents could not remember when symptoms had begun, again highlighting the lack of public awareness of the condition.

Next in the RLS patient journey comes the time it takes for sufferers to realise something is wrong and to seek medical attention. Due to the lack of understanding of the condition, symptoms may initially not be strong enough for sufferers to feel there is a problem, or they may be too embarrassed to seek medical attention as the problem is not severe enough in their opinion.

The PIP Health study found that 56% of those who completed the questionnaire had waited for more than one year to seek medical attention and 16% had waited more than five years. This delay can cause problems as patients with late-onset RLS often experience a more rapid symptom progression, which could, in turn, lead to complications in treatment of symptoms which might have been controlled at an earlier stage.

13 ICM survey data. Conducted Feb 2012
16 Understanding RLS: Why So Many Patients Go Untreated. Video: Patients with Restless Syndrome (RLS) often go for years without a diagnosis, because they either don’t or can’t characterize their symptoms to a doctor. In this video, David Schulman, MD, director of the Emory Sleep Disorders Laboratory in Atlanta.
As David Schulman, MD explains in the video ‘Understanding RLS: Why so many patients go untreated’: ‘RLS is a sensation of discomfort in the legs...it’s usually not painful, it may be pins and needles or they just feel funny’ and this can often be why people tend to wait for some time before consulting a doctor. He goes on to explain: ‘because it’s very difficult for folks with RLS to characterise their discomfort, it’s not painful, so a lot of them don’t go to the doctor about it’.18

The next step in the journey of a patient with RLS is the diagnosis. This stage encompasses the amount of time after medical attention is initially sought to an actual (correct) diagnosis of RLS. During that time evidence suggests that RLS is difficult to diagnose, as highlighted earlier, and it can be hard for a sufferer to characterise their symptoms.18 A clinical diagnosis of RLS can be made only if patients complain of four key symptoms which constitute the essential criteria defined by the International Restless Leg Syndrome Study Group (IRLSSG) in 1995, later refined and reviewed during a National Institutes for Health (NIH) workshop in 2002.19

To be able to diagnose RLS correctly healthcare professionals need to be aware of the disorder and the wide variety of symptoms it can present with. Lack of awareness of what RLS is correlates with a higher probability of misdiagnosis.20

The claim that it can be difficult to diagnose RLS is supported to some degree by the findings in this study that 42% of respondents claimed they were not diagnosed at their initial visit to a healthcare professional and that on average it took 3.59 visits to receive an RLS diagnosis. In addition, 67% of this group of respondents pointed out that it had taken over a year to receive a correct diagnosis. RLS patients frequently cannot relate their sleep problems to the disturbance of their legs and do not report these symptoms,21 which would suggest further knowledge and understanding of RLS about the ways that RLS symptoms could be reported is required by all stakeholders.

Despite RLS affecting 5%-10% of adults in western countries, the condition remains underdiagnosed, and misdiagnosed. So many sufferers wait several years for a correct diagnosis. This is especially the case for patients with chronic RLS that began in childhood.22

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18 Understanding RLS: Why So Many Patients Go Untreated. Video: Patients with Restless Syndrome (RLS) often go for years without a diagnosis, because they either don't or can't characterize their symptoms to a doctor. In this video, David Schulman, MD, director of the Emory Sleep Disorders Laboratory in Atlanta.
In a German population-based survey the overall prevalence of a known doctor diagnosis of RLS was 2.3%, the ratio of diagnosed to undiagnosed RLS was 1:3. In a French study only 5.3% of RLS sufferers received a diagnosis of RLS despite 53% of the sample consulting their doctor with RLS symptoms; 60% of RLS sufferers had previously received a vascular diagnosis mainly related to venous disease. In the REST primary care study in the USA and five European countries, 64.8% of sufferers reported consulting a physician about RLS symptoms, of these only 58% received any diagnosis, while 12.9% were given a diagnosis of RLS; GPs reported that only 37.9% had consulted for RLS symptoms. Similar UK studies gave similar examples of under-diagnosis and mismanagement.

Following diagnosis, the next stage of the RLS patient journey – treatment – can begin. Current RLS treatment is symptomatic, not preventive. To improve quality of life and control of the condition it is important that physicians work closely with, and listen to patients to be able to meet their individual needs and effectively treat the condition.

Some RLS drug formulations do not provide an effect over 24 hours, due to a short drug half-life, and should be administered a few hours before symptoms usually begin in the evening. A patch is newly available that does act for 24 hours. This could potentially be beneficial to a sufferer’s quality of life as the drug does not have to be administered in anticipation of symptoms.

The PIP Health investigation found that 89% of study participants were using RLS treatment at the time of the survey, with the two most common treatments being sleeping aids and antidepressants. This again suggests a level of mismanagement as diagnosed RLS sufferers seem to be being given treatments to aid sleeping to relieve the consequences of insomnia, rather than to manage their RLS. As a consequence they may experience unnecessary side effects which could make their RLS symptoms worse. Also 15% of the group indicated that they had had at least one change in their RLS treatment, with 21% of this group having had three changes made indicating again potential mismanagement of the condition and perhaps difficulty in finding the most effective individual treatment.

The final part of the RLS patient journey in the UK should be viewed as the most important. This stage is the outcome of the journey which includes individual quality of life as a result of all that has gone before, and the effect their condition has on their daily life. Of course, this part of the journey also considers how the condition is controlled: are RLS symptoms relieved, and if so, then the ultimate outcome should be a positive quality of life for the sufferer.

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From a health economic point of view, controlling this stage of the journey effectively could reduce costs. In another study it was determined that average total indirect costs attributable to RLS amounted to EUR 1308 over three months, based on productivity loss.\(^{26}\)

The PIP Health study found that a significant number of those suffering from RLS felt the three main symptoms of the condition had deteriorated since they were initially diagnosed with RLS: 37% of all those who took part highlighted a negative change in ‘sleep disturbance’ with 20% stating a particularly ‘significant’ negative change. Linked to this was the symptom of the ‘urge to move legs’, with 39% experiencing a negative change and 20% again stating that they had felt a ‘significant’ negative change since diagnosis. The final group showed the largest negative change in the symptom ‘uncomfortable/unpleasant sensations in the legs’ with 41% indicating a deterioration and 24% a ‘significant’ negative change. The last two symptoms can, of course, cause the first symptom, ‘sleep disturbance’ which then ultimately has an impact upon daily life and quality of life due to sleep deprivation/insomnia.

Although this is the final part of the RLS patient journey, it may not be the end of the story. For example, if the desired outcome is not achieved then a patient may find the journey takes them back a step to the treatment stage to look at an alternative treatment to achieve an improved quality of life. Or, if misdiagnosed with another condition at the diagnosis stage, a sufferer may find they need to move back to again seek medical attention before receiving a correct diagnosis.

**Figure 4: The RLS patient Journey in the UK.**

![Diagram of the RLS patient journey](image)

The delay in time to diagnosis and the accompanying visits to the GP and other specialists add to the costs associated with this stage in the patient’s journey. In a previous study in Germany, direct and indirect costs were calculated from the perspective of the healthcare and transfer payment providers. The average total cost of a 3-month observation period was EUR 2090, including EUR 780 for health insurance, EUR 300 for drugs, and EUR 354 for hospitalisation costs.\(^{29}\)

Patient data can be considered the optimal data source for a health economic model because it most closely represents the effectiveness of a treatment in a real life setting.

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Especially for factors in health economic models such as quality of life, side effect severity, and rationale for discontinuation, the patients’ perception should be integrated because the patient is the sole source for outcomes related to the patient’s experience with pharmaceutical therapy.\textsuperscript{27}

Using the data from this present study, the average number of visits to the GP (3.59) would cost £89.75 per patient, taking the average cost of a GP visit as £25. Furthermore, misdiagnosis leads to unnecessary specialist referral such as a ‘movement disorder specialist’ or a sleep clinic, which would cost on average £200-225 per visit, with, on average, one or two follow up and/or review appointment(s). This would bring costs to between £489.75 and £714.75 per misdiagnosed patient. If a correct diagnosis was made at the initial visit costs would be considerably lower (eg £25).

In line with the misdiagnosis issues are the related health economic costs; cost-of-illness studies were heterogeneous but indicated that RLS was associated with a substantial economic burden, resulting in high and indirect costs to society.\textsuperscript{28} Furthermore, mistreatment due to misdiagnosis can lead to augmented side effects due to the administration of antidepressants, as shown in this study, where antidepressant treatment was found to be strongly related to substantial productivity losses.\textsuperscript{29}

Limitations and further investigations

As well as how many visits to various healthcare professionals had taken place before an RLS diagnosis was reached, it would have been interesting to look at which were the most common misdiagnoses and what treatments were given as a result and the impact (negative or positive) that may have had before RLS was diagnosed. The study could have examined how participants felt about their misdiagnosis and whether they accepted it as part of the patient journey in order to receive the correct diagnosis.

The study looked at who respondents were referred to but it may have been interesting to investigate further which healthcare professionals had made the referral and look into the reasons given with a series of open-ended questions.

A further study could focus on patients with RLS and what their perceptions are with regards to their condition. A validated ‘Illness Perception Questionnaire’ is available and it could be interesting to do an exercise with a similar group of respondents to segment the patients, which would allow for the provision of the correct treatment, service and

communications to each segment. It would also be interesting to investigate how satisfied people are with the medication and what they would want to see change in their patient journey.

More in-depth analysis may be worthwhile to further understand the importance of a fast diagnosis and treatment plan for RLS in different subgroups within the population. For example, does age or degree of RLS play a role in treatment outcomes?

It was also noted by the researchers that not all treatments currently available for RLS were represented in the study, so more detailed investigation including all available treatments and their positive and negative effects on the outcome of the patient journey would be interesting. This would allow a more precise analysis of the ongoing patient journey in RLS as mapping could be done to explore how frequently patients move forwards and backwards within the different stages of the RLS patient journey.

**Conclusion**

The outcomes of the study lend support to claims that misdiagnosis of RLS is common, and greater knowledge and understanding of the condition from a patient’s point of view is needed. By highlighting the various stages of the patient journey in RLS it is possible to bring the problems associated with each stage to the attention of healthcare professionals and patients.

Greater public awareness of RLS would improve recognition of the condition. Patients may not be embarrassed or unsure whether to seek medical advice if there was greater knowledge surrounding the condition and associated symptoms. If, as a result of greater awareness and understanding, patients sought medical attention earlier the second stage of the journey might be improved as well.

Problems at the diagnosis stage of the patient journey might be reduced through improved knowledge of what the patient is feeling. Healthcare professionals need a deeper understanding of the condition and symptoms its sufferer’s experience. And the sufferers need a deeper understanding to communicate their symptoms more clearly to healthcare professionals and take responsibility for managing their health. Furthermore, understanding patient language and their reasons for suffering from insomnia should improve a physician’s assessment of the problem and reduce the amount of diagnosis time wasted, incorrect treatments prescribed and unnecessary costs incurred.

In summary, earlier diagnosis through improved disease awareness and knowledge and, in turn, earlier effective symptomatic treatment, could lead to an improvement in the quality of life for people with RLS along with a reduction in the associated healthcare costs.

**Disclosure**

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