Background
- Narcolepsy is a chronic neurological disorder characterized by disturbed nocturnal sleep, excessive daytime sleepiness, and symptoms characteristic of disrupted rapid eye movement (REM) sleep, such as cataplexy, sleep paralysis, sleep-related hallucinations, and frequent vivid dreams.
- It is associated with short sleep latency and sleep onset REM periods on the multiple sleep latency test.
- Due to disturbed sleep regulation, individuals tend to sleep instead of fewer instances of sleep and directly enter REM sleep, resulting in less amount of sleep in the N3 sleep stage.
- Sodium oxybate (SXB), the sodium salt of GHB, is the only drug that has demonstrated efficacy across multiple narcolepsy symptom domains, and many randomized controlled trials (RCTs) have shown safety and clinical efficacy in narcolepsy.
- We were interested to examine if the beneficial effects of SXB in patients with narcolepsy are also reported from studies conducted in real-world settings.

Objectives
- To examine the clinical (safety, effectiveness) and humanistic (QoL and other PROs) outcomes associated with SXB when used in the management of narcolepsy in real-world settings.

Methodology

Eligibility Criteria

**Inclusion Criteria**
- 12 months
- E
- 18
- Retrospective observational
- Case
- After treatment
- Adult patients with NC
- Median (Q1-Q3) (Plazzi 2014)
- SXB naïve adults with NT1
- SXB: 267
- S
- Adult male patients with NT1
- 1 yr
- Adult patients with NC
- Cases: 7
- Antelmi 2021
- SD age in years
- 2016
- Mean±SEM (Donjacour 2011-13)
- Prospective observational
- NR
- Mean±SEM (Donjacour 2011-13)
- 24
- 13
- S
- 90
- 3 mths
- Mean±SEM (Donjacour 2011-13)
- 4.1 (SEM)
- 5 d
- Adult patients who received SXB treatment
- Population description
- 12.5
- Children with NC
- Drug naïve children & adolescents with NT1
- Retrospective observational
- Adult male patients with NC
- Leu-Semenescu Q
- Case
- E
- Prospective observational
- 35)
- 2011
- E, E, E
- 11.8
- 16
- E
- 6
- After deduplication
- 17 studies (n = 424)
- Remaining studies: single hospital data
- Mayer 2018: 41 centres in Europe
- Children/ adolescents: 95
- Non-English
- Studies involving adult patients

**Key features of included studies**

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Intervention Dosing</th>
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<tbody>
<tr>
<td>Filardi 2018</td>
<td>SXB treatment increased the proportion of night-time slow wave sleep (2 studies)</td>
</tr>
<tr>
<td>Antelmi 2018</td>
<td>SXB treatment increased the % of time spent awake (2 studies)</td>
</tr>
<tr>
<td>Leu-Semenescu</td>
<td>SXB treatment increased the number of cataplexy events per week (2 studies)</td>
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</tbody>
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**Study design**
- Observational, RWE studies; we excluded RCTs and non-primary studies (such as reviews, editorials, case reports, etc.).

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**Results**
- Total records identified after full-text screening (n = 82)
- Full-text articles excluded for eligibility (n = 58)
- Studies included qualitative analysis of 25 publications from 13 studies

**Safety Outcomes (5 studies)**
- No new safety signals of concern were reported.

**Humanistic Outcomes (2 studies)**
- No new safety signals were noted with the real-world usage of SXB.

**Discussion**
- In the SSR of effectiveness, safety, and humanistic outcomes of SXB in narcolepsy patients in real-world settings, all 17 included studies evaluated effectiveness outcomes, 5 studies evaluated safety outcomes and only 2 studies evaluated humanistic outcomes.
- Only few studies evaluated the same outcomes, resulting in inadequate data to strongly determine improvements in effectiveness, safety, and humanistic outcomes.
- SXB was found to be safe and effective in the treatment of narcolepsy in both adults and children in the real-world setting, and was associated with:
  - Reduction in: Epworth sleepiness score, total sleep time, proportion of REM sleep, wakefulness after sleep onset, and cataplexy
  - Increase in: Sleep efficiency, proportion of slow wave sleep (night and total), proportion of daytime wakefulness, sleep latency
  - Improvement in: Humanistic outcomes such as sleep quality, daytime functioning, HRQoL, PROs
- No new safety signals were noted with the real-world usage of SXB.
- Contrary to our expectation, REM sleep latency was reduced in 4 out of 5 studies; this would require further exploratory analysis.

**Limitations**
- Search was limited to PubMed; databases like Embase was not included.
- Only English language publications were searched.

**Conclusion**
- In line with previous findings of RCTs, SXB was found to be safe and effective in narcolepsy patients treated in real-world settings.
- Future real-world studies need to evaluate standard outcomes consistently to enable pooling and collective analysis of data that can lead to more conclusive evidence on the effectiveness and safety of SXB in narcolepsy.

References