Central Sleep Apnoea during CPAP therapy
First insights from a big data analysis
Big data: a complementary approach to clinical trials to explore clinical challenges

<table>
<thead>
<tr>
<th>Big data (real-life massive data)</th>
<th>Clinical trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>✅ Includes <strong>as broad a sample</strong> as possible and can explore questions of clinical relevance that cannot be answered using small patient populations found in clinical trials(^1,^2,^3)</td>
<td>✅ Offer a very <strong>controlled environment</strong> for examining hypotheses and minimising uncertainties</td>
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<tr>
<td>✅ Identifies <strong>signals or trends</strong>, undetectable in smaller data samples, and generates hypotheses</td>
<td>✅ Define a <strong>precise</strong> patient population</td>
</tr>
<tr>
<td>✗ Difficult to rule out unidentified confounders; <strong>uncertainties</strong> cannot be eliminated</td>
<td>✗ Randomised controlled trials exclude most patients seen in routine clinical practice, and the <strong>findings rarely mirror clinical practice</strong></td>
</tr>
</tbody>
</table>

These two approaches are complementary and together can provide a better understanding of the question at hand and **minimise the limitations of each methodology**.
Big data provides an effective tool for small populations such as Complex Sleep Apnoea (CompSA) or emergent Central Sleep Apnoea (CSA) patients.

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A study of CSA/CompSA looked at anonymous data from PAP devices in the US\textsuperscript{1}

- Patients agreed to be telemonitored, and data were de-identified and aggregated. As US data protection laws\textsuperscript{2} allow the use of device data for scientific purposes if de-identified, an institutional review board waiver was provided and patient informed consent was not necessary in this study.

- A random sample representing 30\% of the database population that began CPAP or APAP in 2015 was analysed. Of the initial patient population of 189,946, 133,006 used a PAP device ≥ 1 day with use ≥ 1 hour in Week 1 and Week 13 (inclusion criteria).

- The definition used for residual CSA was CAI ≥ 5/h, calculated in 1-week assessment windows. This differs from previous research because it introduces repeated measures based on real-life telemonitoring data rather than single “snapshots” of CSA.

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1 Liu et al. Trajectories of emergent central sleep apnea during continuous positive airway pressure therapy. *Chest.* 2017;152(4):751-60

2 The United States Privacy Act, the Safe Harbor Act and the Health Insurance Portability and Accountability Act
Three categories of CompSA were identified: emergent, transient, and persistent CSA.

Using the threshold of residual CAI ≥ 5/h, 3.5% of the patients had CSA at day 1 or day 90 of CPAP therapy:

- **Patients with OSA** had an average CAI that remained consistently well below the threshold of 5 CSA events per hour.
- **Patients with transient CSA** began above the threshold but then gradually normalised over the 90-day period.
- **Patients with emergent CSA** began below the cut-point of 5/h, but rose gradually over time.
- **Patients with persistent CSA** remained consistently well above the cut-point.

Similar trends were observed when day-by-day values of CAI and AHI over the first 2 weeks of therapy were analysed.

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1 Liu et al. Trajectories of emergent central sleep apnea during continuous positive airway pressure therapy. *Chest*. 2017;152(4):751-60
These findings remain consistent using either the ERS or the US definition of persistent CSA (AHI ≥ 15/h or CAI ≥ 5/h).

- The initial analysis was done according to the US definition of residual or persistent CSA, which is CAI ≥ 5/h. The recent European Respiratory Society (ERS) task force states that patients with persistent CSA with a persistent AHI ≥ 15/h should be switched to ASV.* The investigators also performed a post-hoc analysis using this definition to look at any differences.

When using this more restrictive ERS task force criteria, the prevalence of residual CSA differs slightly (1.2%). However, all other findings are similar.

- Only one of the terms, emergent CSA, is currently recognised as a new category of CSA by the International Classification of Sleep Disorders-Third Edition¹ and the ERS task force document on central breathing disturbances.² However, this study seems to show that we can indeed identify 3 categories.

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* ASV therapy is contraindicated in patients with chronic, symptomatic heart failure (NYHA 2-4) with reduced left ventricular ejection fraction (LVEF ≤ 45%) and moderate to severe predominant central sleep apnoea.

Each category of CompSA is associated with decreased compliance and increased therapy drop-out risk\(^1\)

- **Average daily usage hours** in the first 90 days were lower in those with any kind of CSA during CPAP therapy than in those without.

- Patients with any CSA during CPAP were significantly more likely to terminate therapy after 90 days than those without CSA.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Therapy termination more likely</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease Phenotype</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>OSA</td>
<td></td>
<td>1.000</td>
<td>1.000</td>
<td>0.007</td>
</tr>
<tr>
<td>Transient CSA</td>
<td></td>
<td>1.289</td>
<td>1.143</td>
<td>1.408</td>
</tr>
<tr>
<td>Persistent CSA</td>
<td></td>
<td>1.481</td>
<td>1.283</td>
<td>1.709</td>
</tr>
<tr>
<td>Emergent CSA</td>
<td></td>
<td>1.721</td>
<td>1.486</td>
<td>1.993</td>
</tr>
</tbody>
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Patients with emergent CSA were nearly 2 times more likely to terminate CPAP therapy than OSA patients on day 90.
Compared with the OSA group, patients with any CSA during CPAP therapy were less likely to continue using therapy. The estimated probability of continuing CPAP therapy on day 300 was:
- 83% for OSA,
- 79% for transient CSA
- 76% for persistent CSA
- 72% for emergent CSA.

All forms of CSA negatively impact CPAP therapy, decreasing compliance and increasing therapy drop-out risk. The same trajectories impact compliance or therapy termination risk similarly whether identified using ERS task force criteria or US criteria.
Switching from CPAP to ASV in patients with emergent or persistent CSA may improve adherence\(^1\)

A **second analysis** was performed with a random sample representing 30% of the database population that had begun CPAP therapy or ASV therapy from 1 Jan to 2 Oct 2015 plus all who switched from CPAP to ASV over the same period. Adherence (US Medicare definition\(^1\)) and device usage were determined for 3 groups: started on CPAP and stayed on CPAP (CPAP only; \(n = 189,724\)), started on ASV and stayed on ASV (ASV only; \(n = 8,957\)), started on CPAP and switched to ASV (\(n = 209\)).

- **Average PAP usage hours increased** after ASV switch.
- **Average AHI decreased** after ASV switch.

### Average PAP usage hours before vs after CPAP to ASV switch

* Adherence to CPAP is defined as usage greater or equal to 4 hours per night on 70% of nights during a consecutive 30 days anytime during the first 3 months of initial usage.

These data suggest that normalisation of CSA during CPAP (transient CSA) may contribute to better long-term adherence to CPAP therapy.

However, if there is persistence of CSA after 2 weeks*, then the patient fits within the trajectory of emergent or persistent CSA as shown by these data and will probably require a switch to ASV.

These data are in line with the recent recommendations of the ERS, which state that in patients with persistent CSA and AHI ≥ 15 events per hour, ASV is the appropriate therapy.

* Similar trends were observed when day-by-day values of CAI and AHI over the first 2 weeks of therapy were analysed.

Patients who experience emergent or persistent CSA while on CPAP therapy may benefit from a switch to ASV.

Patients who experience transient CSA with subsequent normalisation may continue on CPAP therapy.

Adherence rate improved immediately after patients with emergent or persistent CSA switched from CPAP to ASV.

<table>
<thead>
<tr>
<th></th>
<th>CPAP only</th>
<th>ASV only</th>
<th>CPAP to ASV switch</th>
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<tbody>
<tr>
<td>90 day adherence rate</td>
<td>73.8%</td>
<td>73.2%</td>
<td>76.6%</td>
</tr>
<tr>
<td>n</td>
<td>189,724</td>
<td>8,957</td>
<td>209</td>
</tr>
<tr>
<td>Adherence improvement in the two patient subgroups that switched from CPAP to either fixed (n = 127, p &lt; 0.05) or variable (n = 82, p &lt; 0.01) EPAP ASV.</td>
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</table>
Identify residual CSA with ResScan™

The statistical data of ResScan provide the AHI, AI, CAI, HI and ODI (if used with an oximeter), which allows you to identify residual CSA and CSR during CPAP therapy.

1. Log into ResScan
2. Go to patient record
3. Go to “Settings”
4. Check that your patient is on CPAP/APAP therapy by looking at the Therapy mode
5. Go to “Statistics”
6. Select the last 2 weeks
7. Look at AHI & AI to see if: AHI ≥ 15/h, AI > 5/h or CAI > 5/h
Identify residual CSA with AirView™

AirView colour-coded wireless dashboard allows you to easily identify low usage and residual AHI. It provides an overview of the usage, AHI and leakage of the last 10 days. AirView icon guide is available on the AirView welcome page under “Resources” at the bottom of the page.

1. Log into AirView
2. Go under the patients tab and then click on wireless selection to access the wireless dashboard
3. Look at your patients on CPAP/APAP therapy
4. Look at patients with these icons:
   - High AHI
   - High AHI, leak data not supported
5. Click on the square indicating a too high AHI to see detailed data
6. Look at AHI to see if AHI ≥ 15/h
7. Click on the patient
8. Go to “Create report” and select “Compliance & Therapy report”
9. Go through the report and look for CAI to see if CAI > 5/h
ResMed Air Solutions devices to treat Sleep Apnoea

Adaptive Servo-Ventilation device for the treatment of Central Sleep Apnoea; stabilises the ventilation of adult patients, with or without associated obstructive events. Reduced LVEF should be excluded before starting ASV. Before using ASV, it is important to ensure that LVEF is >45%.* Echocardiography is recommended for this purpose.

Positive Airway Pressure devices for the treatment of Obstructive Sleep Apnoea with integrated remote monitoring (patient weighing more than 30 kg). These devices feature Forced Oscillation Technique (FOT) technology to classify residual events as obstructive or central, as well as a Cheyne-Stokes Respiration detection algorithm.

Software to manage the therapy of patients treated with ResMed’s positive airway devices.

*Contraindication: ASV therapy is contraindicated in patients with chronic, symptomatic heart failure (NYHA 2-4) with reduced left ventricular ejection fraction (LVEF ≤ 45%) and moderate to severe predominant central sleep apnoea.

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