A Scientometric Review of Obstructive Sleep Apnea and Obesity

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Abstract: Obstructive sleep apnea (OSA) is a common sleep disorder that has a high prevalence in the obese population. Studies have established the relationship between OSA and a multitude of adverse health outcomes including cardiovascular diseases and metabolic diseases, indicating the nature of OSA as a disorder with high comorbidity and mortality. Thus, OSA is a growing public health concern in the face of rising obesity trends globally. This study conducted a systematic analysis of the scientific literature on OSA from 1977 to 2022 in order to gain a better understanding of major research areas concerning OSA and the connections between these areas. Findings indicate that there are major clusters investigating the relationship between OSA and cardiovascular and metabolic diseases, which are health conditions commonly associated with obesity and have a significant disease burden. The findings from this scientometric analysis also indicate emerging clusters of research into more specific populations such as children with obesity and pregnant women.

Keywords: obstructive sleep apnea; obesity; scientometrics

1. Introduction

Obstructive sleep apnea (OSA) is a condition involving repeated episodes where the upper airway completely or partially collapses, which often leads to oxygen desaturation or sleep arousal [1,2]. There have been many studies indicating the high prevalence of OSA across many different populations as well as subgroups (e.g., [3–9], see [10,11] for reviews). For example, a systematic review by Senaratna et al. [10] found that the overall prevalence of sleep apnea ranged from 9 to 38% for ≥5 events/hour apnea–hypoapnea index (AHI), where the AHI is a major index of the severity of sleep apnea. Moreover, the prevalence of OSA has been on the rise in recent times and affects both developed and developing countries [12]. This worrying trend is a cause of concern due to the adverse health outcomes and mortality associated with OSA.

OSA has been linked with many clinical health conditions, including hypertension as well as cardiovascular and metabolic diseases [13–15]. In particular, the Sleep Heart Health Study was one of the first studies to examine the association between OSA and cardiovascular disease and found modest to moderate associations between sleep-disordered breathing and cardiovascular disease [16]. Notably, Marin et al. [17] found that severe OSA led to a significant increase in risk of both fatal and non-fatal cardiovascular events. Many studies have also demonstrated independent associations between sleep apnea and increasing insulin resistance [8,13,18], although there have been inconsistent results surrounding the association between OSA and diabetes [14,19,20]. Hence, there is increasing recognition of OSA as a major public health burden in and of itself, alongside its contribution to the development of cardiovascular, metabolic, and psychiatric disorders.

One factor contributing to the increase in OSA is the increasing obesity rates. Across the globe, obesity rates have doubled since 1980 [21], and recently, the United States of
America has reported that the prevalence of obesity in adults was 41.9% [22]. Obesity has been established in many studies as one of the strongest risk factors of OSA [3,8,10,23–25]. For example, there is evidence from a follow-up of the Wisconsin Sleep Cohort Study demonstrating that a 10% change in body weight is associated with an accompanying increase in approximately 30% in the AHI [24]. Similarly, Newman et al. [26] demonstrated relations between modest changes in weight and sleep-disordered breathing, where men with ≥10 kg weight gain were approximately five times more likely to show a large increase in the respiratory disturbance index. There are a number of factors linking obesity to sleep apnea. First, the increased parapharyngeal fat deposit and neck fat results in upper airway obstruction during sleep through the narrowing of the airway [27,28]. Second, increased abdominal girth and a lying position result in a decrease in lung volume, which exacerbates the hypoxia through the reduction of traction on the upper airway [29]. Third, upper airway collapsibility has been found to be higher in obese individuals compared to nonobese individuals [30]. Fourth, obesity has been proposed to modulate neuromuscular control in the upper airway [28]. Given the continuing rise in obesity rates across the globe, it can be expected that OSA will continue to grow as a public health concern, further exacerbating health problems commonly associated with obesity.

The aim of this study is the identification of key publications in the literature on OSA and obesity, the main thematic trends, and existing gaps using a data-driven approach. To do so, a document co-citation analysis (DCA) was conducted [31,32]. From the results of the scientometric analysis, publication trends and the links between individual works can be derived.

2. Materials and Methods

2.1. Data Collection from Scopus

In line with the standard and established scientometric procedures [31,33], publications were downloaded from Scopus using the following search string TITLE-ABS-KEY (“obstructive sleep apnea” AND “obes*”) AND (LIMIT-TO (LANGUAGE, “English”)). A total of 6056 documents published from 1 January 1977 to 14 September 2022 were found. The limitation of the search to English publications allows for a more standardised and rigorous analysis of the work, as it will be built on scientific literature on an international scale [34].

2.2. Data Eligibility

The articles downloaded from Scopus were imported into CiteSpace software (Version 6.1.R2), which was used to conduct the scientometric analysis. The software identified a total of 275,741 references cited by the 6056 articles retrieved from Scopus. Of the total number of references, 272,574 (98.85%) were considered valid by the software (Figure 1). CiteSpace considers as valid only the references with all of the following seven key pieces of information: author, year of publication, title, source, volume, pages, and DOI [31]. Irregularities in the citation format led to a number of references being considered “invalid”. Such negligible losses in references (1–5%) are a common occurrence due to incorrect citation formats when data are being imported into CiteSpace [35]. In order to remove identical or repeated entries, the CiteSpace function Remove Alias was turned ON.

2.3. Document Co-Citation Analysis (DCA) on the Eligible References

A DCA was conducted to determine the main research domains in the literature on obstructive sleep apnea, on the sample of articles downloaded from Scopus, and on their valid references. DCA examines the frequency with which two or more papers are cited together in source articles [36]. The assumption of DCA is that common research trends and intellectual domains in the literature are reflected by frequent co-citations among articles [32,37]. From the DCA, a network consisting of documents which are frequently cited together and the documents that cite them (i.e., articles downloaded from Scopus) is constructed.
In the current study, DCA parameter optimization was conducted in order to obtain a balanced network of documents. This was carried out by computing and comparing several DCAs, each with a different setting for one of three node selection criteria: g-index, TOP N, and TOP N%, as conducted in [33,34,37–40]. The node selection criteria refer to a priori settings defining the criterion employed for the selection of articles to be included in the network, which then determine the final network of articles being generated. The g-index is a measure of the citation scores of an author’s top publications [41,42]. The g-index value represents the largest number equal to the average number of citations of the most highly cited g publications [35]. TOP N and TOP N% are criteria used to select N and N% most cited within a time slice—set as 1 year in this study—as network nodes, respectively [31]. The time slice was kept constant at the value of 1 year because we were interested in conducting the analysis on a year-by-year basis to obtain the maximum amount of information.

DCAs with variations in node selection criteria and their scale factor values, which refer to the chosen numeric values used as thresholds for the respective node selection criteria [40], were computed for the generation of the final optimal network. Specifically, DCAs with the following node selection criteria were compared: g-index with scale factor k set at 15 and 25, TOP N with scale factor N set at 25, 50 and TOP N% with scale factor N set at 10, where g-index with k = 25, TOP N with N = 50, and TOP N% with N = 10 represents the default scale factors. These values were initially selected and varied to optimize the structural parameters of the network (i.e., modularity, silhouette, number of nodes, and number of clusters). This procedure follows CiteSpace’s recommendations, and it has also been adopted in previous publications [31,33,34,37–40]. A DCA with a g-index with the scale factor k set to 25 was the parameter used to generate the final network of articles after these metrics were compared.

2.4. Metrics to Evaluate the Results

There are two types of metrics—structural and temporal—used in the description of the results from CiteSpace. Structural metrics include the following: (i) modularity-Q, (ii) silhouette scores and (iii) betweenness centrality. The modularity-Q value has a range from 0 to 1 and indicates the degree to which the network can be decomposed into single
groups of nodes, which are referred to as modules or clusters [43]. A well-structured network is indicated by a high modularity-Q value [32]. Silhouette scores are a measure of inner consistency of modules in terms of internal cohesion and separation from other clusters [44]. Silhouette scores have a range from $-1$ to $+1$, where higher values represent high separation from other modules and internal consistency [45]. Betweenness centrality represents the degree to which a node connects an arbitrary pair of nodes in the network [31,46]. Betweenness centrality values range from 0 to 1, where higher scores are usually observed for ground-breaking and revolutionary works in the scientific literature [43].

Temporal metrics consist of (i) citation burstness and (ii) sigma. Citation burstness is calculated using the Kleinberg’s algorithm [47]. The citation burstness is indicative of a sudden increase in the number of citations of an article within a given time frame [48]. Sigma is calculated with Equation $(\text{centrality} + 1)^{\text{burstness}}$ and indicates the novelty of a document and influence on the overall network [49].

Modularity-Q and silhouette scores were used to examine the overall configuration of the generated network and identified clusters of references. Betweenness centrality and the temporal metrics were used in examining the attributes of single nodes in the network.

3. Results

3.1. Structural Metrics

The final optimised network obtained from the DCA consisted of 2026 nodes with 9267 links, which indicates an average of 4.57 connections with other references for each node (Figure 2). The network had a modularity-Q index of 0.779 and a mean silhouette score of 0.905, indicating high divisibility into homogeneous clusters of the network.

![Figure 2. Network of documents generated through the document co-citation analysis (DCA). The major clusters are highlighted and divided by colour. The following articles are shown in the figure: Young et al. [3], Marin et al. [17], Young et al. [25], Peppard et al. [50], Berry et al. [51], Gupta et al. [52], Buchwald et al. [53], Tauman and Gozal [54], Howard et al. [55], Jordan et al. [56], Mathur et al. [57].](image)

3.2. Thematic Clusters

A total of 13 major clusters were identified in the final optimised network (Figure 2, Table 1). For each cluster, a label was generated by means of the CiteSpace’s log-likelihood ratio (LLR) algorithm. A qualitative inspection of clusters was conducted to assess the accuracy of LLR labels. Where LLR labels lacked accuracy, clusters were renamed manually based on the documents they included [33]. The largest cluster #0 consisted of 320 nodes and
had a silhouette score of 0.892, with the constituent references being published in 2005 on average. The cluster was manually labelled “Clinical implications of OSA”. Second, cluster #1 consisted of 245 nodes and had a silhouette score of 0.804, with the constituent references being published in 2014 on average. The cluster was manually labelled “Metabolic disorders and OSA”. Third, cluster #2 consisted of 175 nodes and had a silhouette score of 0.968, with the constituent references being published in 1998. The cluster was manually labelled “Diagnosis and clinical presentation of OSA”. Clusters #21, #2, and #0 had the oldest mean years of publication (1997, 1998, and 2005, respectively) whereas clusters #23, #20, and #3 were the most recent clusters with the mean years of publication of 2021, 2020, and 2018, respectively.

**Table 1.** Metrics of the 13 clusters identified with the document co-citation analysis (DCA). Log-likelihood ratio (LLR) labels are automatically generated by the software.

<table>
<thead>
<tr>
<th>Cluster ID</th>
<th>Size</th>
<th>Silhouette</th>
<th>Mean Publication Year</th>
<th>SD Publication Year</th>
<th>Mode Publication Year</th>
<th>LLR Label</th>
<th>Suggested Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>320</td>
<td>0.892</td>
<td>2005</td>
<td>3.29</td>
<td>2005</td>
<td>Metabolic syndrome</td>
<td>Clinical implications of OSA</td>
</tr>
<tr>
<td>1</td>
<td>245</td>
<td>0.804</td>
<td>2014</td>
<td>3.35</td>
<td>2009</td>
<td>Risk factor</td>
<td>Metabolic disorders and OSA</td>
</tr>
<tr>
<td>2</td>
<td>175</td>
<td>0.968</td>
<td>1998</td>
<td>2.57</td>
<td>1994</td>
<td>Airway management</td>
<td>Diagnosis and clinical presentation of OSA</td>
</tr>
<tr>
<td>3</td>
<td>167</td>
<td>0.896</td>
<td>2018</td>
<td>3.34</td>
<td>2015</td>
<td>Goal questionnaire</td>
<td>Epidemiology of OSA</td>
</tr>
<tr>
<td>4</td>
<td>136</td>
<td>0.937</td>
<td>2017</td>
<td>3.32</td>
<td>2014</td>
<td>Pediatric obstructive sleep apnea</td>
<td>Pediatric obstructive sleep apnea</td>
</tr>
<tr>
<td>5</td>
<td>105</td>
<td>0.925</td>
<td>2008</td>
<td>3.28</td>
<td>2004</td>
<td>Greek children</td>
<td>Childhood obesity and OSA</td>
</tr>
<tr>
<td>6</td>
<td>98</td>
<td>0.919</td>
<td>2017</td>
<td>2.83</td>
<td>2014</td>
<td>Anaesthesia surgery</td>
<td>OSA during pregnancy</td>
</tr>
<tr>
<td>7</td>
<td>97</td>
<td>0.959</td>
<td>2010</td>
<td>2.12</td>
<td>2005</td>
<td>Cardiovascular disorder</td>
<td>Cardiovascular diseases and OSA</td>
</tr>
<tr>
<td>9</td>
<td>54</td>
<td>0.967</td>
<td>2006</td>
<td>3.05</td>
<td>2004</td>
<td>Bariatric surgery</td>
<td>Bariatric surgery and OSA outcomes</td>
</tr>
<tr>
<td>20</td>
<td>11</td>
<td>0.991</td>
<td>2020</td>
<td>2.79</td>
<td>2019</td>
<td>Obesity hypventilation syndrome</td>
<td>Obesity hypoventilation syndrome</td>
</tr>
<tr>
<td>21</td>
<td>10</td>
<td>0.999</td>
<td>1997</td>
<td>2.16</td>
<td>1995</td>
<td>Obese</td>
<td>Upper airway obstruction in OSA</td>
</tr>
<tr>
<td>23</td>
<td>10</td>
<td>0.993</td>
<td>2021</td>
<td>2.16</td>
<td>2017</td>
<td>Adolescent patient</td>
<td>Biological markers of OSA</td>
</tr>
<tr>
<td>43</td>
<td>4</td>
<td>1</td>
<td>2006</td>
<td>2.5</td>
<td>2001</td>
<td>Bariatric surgery patient</td>
<td>Surgical procedures in OSA patients</td>
</tr>
</tbody>
</table>

3.3. Citation Burstness

A total of 402 documents exhibited a citation burst (Table 2). Out of these 402 documents, 129 of them belong to cluster #0, 81 to cluster #1, 20 to cluster #2, 36 to cluster #3, 32 to cluster #4, 29 to cluster #5, 19 to cluster #6, 36 to cluster #7, 15 to cluster #9, and 1 from cluster #43. The article with the strongest citation burst was authored by Peppard et al. [50] with a score of 54.94, with the burst beginning in 2015 to 2022. Hence, this article represents the most impactful publication in the field of OSA and obesity. Furthermore, there were five articles with the longest burst duration of 8 years: [24] from 2000 to 2008 and [58–61] from 2014 to 2022. These documents were the ones that remained impactful for the longest period within the examined literature. Finally, the article with the highest sigma value was
authored by [24], with a sigma value of 20.84. This article was thus regarded as novel and highly influential in the research on OSA and obesity.

Table 2. Top 15 publications in terms of burst strength.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Citation Burstness</th>
<th>Publication Year</th>
<th>Burst Begin</th>
<th>Burst End</th>
<th>Duration</th>
<th>Betweenness Centrality</th>
<th>Sigma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peppard et al. [50]</td>
<td>54.94</td>
<td>2013</td>
<td>2015</td>
<td>2022</td>
<td>7</td>
<td>0.05</td>
<td>14.8</td>
</tr>
<tr>
<td>Berry et al. [51]</td>
<td>46.85</td>
<td>2012</td>
<td>2015</td>
<td>2020</td>
<td>5</td>
<td>0.02</td>
<td>2.03</td>
</tr>
<tr>
<td>Peppard et al. [24]</td>
<td>44.2</td>
<td>2000</td>
<td>2000</td>
<td>2008</td>
<td>8</td>
<td>0.07</td>
<td>20.84</td>
</tr>
<tr>
<td>Young et al. [25]</td>
<td>38.57</td>
<td>2002</td>
<td>2003</td>
<td>2010</td>
<td>7</td>
<td>0.04</td>
<td>4.05</td>
</tr>
<tr>
<td>American Academy of Sleep Medicine Task Force [1]</td>
<td>37.86</td>
<td>1999</td>
<td>2001</td>
<td>2007</td>
<td>6</td>
<td>0.01</td>
<td>1.62</td>
</tr>
<tr>
<td>Marcus et al. [62]</td>
<td>33.29</td>
<td>2012</td>
<td>2014</td>
<td>2020</td>
<td>6</td>
<td>0.03</td>
<td>2.56</td>
</tr>
<tr>
<td>Shahar et al. [16]</td>
<td>32.62</td>
<td>2001</td>
<td>2003</td>
<td>2009</td>
<td>6</td>
<td>0.01</td>
<td>1.38</td>
</tr>
<tr>
<td>Senaratna et al. [10]</td>
<td>30.19</td>
<td>2017</td>
<td>2018</td>
<td>2022</td>
<td>4</td>
<td>0.01</td>
<td>1.17</td>
</tr>
<tr>
<td>Young et al. [3]</td>
<td>29.85</td>
<td>1993</td>
<td>1996</td>
<td>2001</td>
<td>5</td>
<td>0.02</td>
<td>1.62</td>
</tr>
<tr>
<td>Ip et al. [5]</td>
<td>29.01</td>
<td>2002</td>
<td>2003</td>
<td>2010</td>
<td>7</td>
<td>0.02</td>
<td>1.86</td>
</tr>
<tr>
<td>Marin et al. [17]</td>
<td>28.76</td>
<td>2005</td>
<td>2006</td>
<td>2013</td>
<td>7</td>
<td>0.01</td>
<td>1.52</td>
</tr>
<tr>
<td>Heinzler et al. [4]</td>
<td>27.7</td>
<td>2015</td>
<td>2016</td>
<td>2022</td>
<td>6</td>
<td>0.02</td>
<td>1.62</td>
</tr>
<tr>
<td>Punjabi et al. [8]</td>
<td>27.36</td>
<td>2002</td>
<td>2003</td>
<td>2010</td>
<td>7</td>
<td>0.02</td>
<td>1.93</td>
</tr>
<tr>
<td>Vgontzas et al. [18]</td>
<td>26.54</td>
<td>2002</td>
<td>2003</td>
<td>2010</td>
<td>7</td>
<td>0.01</td>
<td>1.17</td>
</tr>
<tr>
<td>Kapur et al. [63]</td>
<td>24.46</td>
<td>2017</td>
<td>2019</td>
<td>2022</td>
<td>3</td>
<td>0.01</td>
<td>1.29</td>
</tr>
</tbody>
</table>

4. Discussion

Each cluster will be discussed in greater detail in this section according to the chronological order in terms of the average year of publication of the cluster. This allows us to identify the main trends of research that mark the conceptual evolution of the research in OSA and obesity [64]. The analysis of each cluster will include the citing articles and cited references, where we will highlight the main citing articles in each cluster along with the coverage and global citing score (GCS). Coverage refers to the number of articles in the cluster that were cited by the citing article and GCS refers to the total number of citations received by a paper as indexed on Scopus.

4.1. Cluster #21: Upper Airway Obstruction in OSA

The two major citing articles in Cluster #21 were authored by Schwab [65] with a coverage of seven articles and a GCS of 154 and Kyzer and Charuzi [66], with a coverage of four articles and a GCS of 109. Cluster #21 appears to be one of the earlier groups of work examining the pathogenesis of OSA in terms of upper airway anatomy and obstruction, as observed from its mean year of publication (1997). In order to address the lack of knowledge on the mechanisms underlying OSA in those times [65,66], Schwab [65] discusses the utility of emergent upper airway imaging and different imaging modalities. As argued by the author, in that period, imaging techniques began to prove useful in providing anatomic data and evidence to better understand the mechanisms of OSA and to evaluate the basis of successful therapeutic interventions. The strength of imaging techniques lies in their ability to map soft tissue and bony structures, which are pivotal to understand changes in respiration, sleep, and airway obstruction in OSA. In a similar vein, the majority of cited references were studies examining at the anatomic factors of OSA [67–70]. In particular, Bacon et al. [69] and Suto et al. [70] used medical imaging to obtain a morphological characterisation and to localise the sites of pharyngeal airway obstruction in patients with sleep apnea, respectively. For instance, Bacon et al. [69] observed that people with sleep apnea syndrome are characterised by elongated soft palate, smaller sagittal dimensions of upper face and anterior cranial base, and retruded chin and tongue. Furthermore, results showed that the dimensions of the upper face and of the anterior cranial base were negatively correlated with the bony pharynx opening.
4.2. Cluster #2: Diagnosis and Clinical Presentation of OSA

The major citing articles in cluster #2 were authored by Koenig [71] with a coverage of 28 articles and a GCS of 336; Strohl and Redline [72] with a coverage of 21 articles and a GCS of 377; and Redline and Strohl [73] with a coverage of 18 articles and a GCS of 31. The main theme of cluster #2 appears to be the diagnosis and identification of patients with sleep apnea as observed from these major citing articles, which promote moving away from viewing OSA as a predominantly male condition occurring in those with obesity and relying solely on polysomnography results. Instead, there is a wide spectrum in terms of the clinical presentation of OSA, with many patients that are not diagnosed with the disorder or that are diagnosed too late. In line with the cluster, to tackle this problem, Skomro and Kryger [74] argued that clinicians should put effort in identifying the risk factors for OSA. Furthermore, the same authors suggest that the clinical evaluation should include a profound examination of the upper airway. Similarly, the cluster focuses on recognition of risk factors such as being male, age, family history, snoring, neck circumference, and clinical presentations of OSA which are not restricted to excessive daytime sleepiness as can be observed from a majority of the citing (e.g., [72–78]) and cited (e.g., [79–83]) articles in the cluster. In fact, respiratory failure and daytime somnolence in some cases might even be absent at the beginning of the disorder [74]. The research on the clinical features of people with OSA in the cluster aimed to highlight the heterogeneity in the clinical presentation of the disorder and to address the reported under-recognition of OSA in the general population.

4.3. Cluster #0: Clinical Implications of OSA

The major citing articles in Cluster #0 were authored by Zamarrón et al. [84], with a coverage of 50 articles and a GCS of 2; Lurie [85], with a coverage of 47 articles and a GCS of 8; and Parati et al. [86], with a coverage of 44 articles and a GCS of 158. Cluster #0 is the largest cluster, which appears to be an immense body of work revolving around the study of the clinical implications of OSA in terms of the relationships between OSA and cardiovascular and metabolic diseases such as heart failure and type 2 diabetes mellitus. As reported by Zamarrón et al. [84], during respiratory failures in OSA, patients experience instances of hypoxia and reoxygenation, which provoke systemic damages in the organism. In fact, as argued by the authors, OSA emerges as an independent factor in the pathogenesis of cardiovascular disorders, and it is often linked with the onset and progression of heart failure. Accordingly, further evidence suggests that OSA has been established to result in sympathetic activation, systemic inflammation, and endothelial dysfunction, which are markers of cardiovascular risk (see [59] for a review). Intermittent hypoxia and sleep fragmentation due to OSA contribute to sympathetic activation and catecholamine release, causing glycogenesis and insulin resistance (see [19,59] for reviews). The size of the cluster attests to the public health burden that OSA carries due to the cardiovascular and metabolic consequences of this condition as well as the corresponding research and attention given to the study and understanding of OSA. Notably, many of the citing articles (e.g., [87–92]) as well as the cited references (e.g., [5,8,16,17,93,94]) examined either cardiovascular or metabolic consequences or both.

4.4. Cluster #43: Surgical Procedures in OSA Patients

The major citing articles in cluster #43 were authored by Givelber and Sanders [95], with a coverage of 3 articles and a GCS of 0; Krieger and Caples [96], with a coverage of 3 articles and a GCS of 0; and Trakada et al. [97], with a coverage of 2 articles and a GCS of 40. Cluster #43 appears to be a cluster of work regarding adverse outcomes which may occur during an operation where the patient is under anaesthesia due to difficult in airway maintenance as observed from the citing articles by Givelber and Sanders [95], Isono [98], and Inge et al. [99]. For example, Givelber and Sanders [95] highlighted the importance of both perioperative management including anaesthesia technique, airway management, and patient monitoring in patients undergoing bariatric surgery. Bariatric surgery is a weight
loss intervention conducted to treat obesity and its comorbidities, such as OSA [100]. In the
group of patients undergoing bariatric surgery, perioperative management is important
because existing upper airway obstruction may be further worsened by loss in tone from
anaesthesia. Similarly, postoperation complications have been reported where there may
be pulmonary and cardiac complications due to hypoxemic episodes, which may be exacer-
bated by the rebound in rapid eye movement sleep as sleep patterns are re-established, and
may even lead to death [95,101].

The cluster is likely to have emerged in response to the release of practical guidelines
by the American Society of Anaesthesiologists Task Force for the management of patients
with OSA in 2006 which coincides with the mean year of publication of this cluster. Notably,
this report by the American Society of Anaesthesiologists is one of the cited references [101],
a long with a study on postoperative complications in OSA patients [32].

4.5. Cluster #9: Bariatric Surgery and OSA Outcomes

The major citing articles in cluster #9 were authored by Givelber and Sanders [95],
with a coverage of 11 articles and a GCS of 0; Olson and Courcoulas [102], with a cov-
 erage of 10 articles and a GCS of 0; and Kapsimalis and Kryger [103], with a coverage
 of 9 articles and GCS of 113. In line with the work of previous clusters identifying over-
 weight and obese individuals as a population at risk of OSA, the cluster appears to be
extending previous work by investigating the effects of bariatric surgery and weight loss
on OSA outcomes, which generally indicate an improvement in OSA symptoms with weight
loss [95]. It also appears to be an offshoot from cluster #43 into the niche of bariatric
surgery, which can be expected considering that OSA is extremely common in patients who
undergo bariatric surgery (see [95]). A majority of the citing articles are clinical studies
reporting the OSA outcomes of bariatric surgery patients (e.g., [100,104–107]) including a
meta-analysis on of the effects of surgical weight loss on OSA by Greenburg et al. [108]. No-
tably, the meta-analysis by Greenburg et al. [108] found that although there is a significant
reduction in the AHI, the mean AHI after surgery was found to be consistent with OSA
of moderate severity, suggesting that bariatric surgery is not a direct cure for OSA. Simi-
larly, many cited references also discuss bariatric surgery and post-surgery OSA outcomes
(e.g., [53,109–114]). The formation of the cluster is also likely to have been catalysed by the
development and validation of the STOP questionnaire, which assesses snoring, tiredness
during daytime, observed apnea, and high blood pressure (STOP), and is used to screen for
OSA in surgical patients.

4.6. Cluster #5: Childhood Obesity and OSA and Cluster #4: Pediatric Obstructive Sleep Apnea

Cluster #5 and cluster #4 will be discussed together in this section as they both
address OSA in childhood. However, they do so under a different light. On the one hand,
documents in cluster #5 discuss the occurrence and the clinical manifestations of OSA in
childhood. On the other hand, documents in cluster #4 were interested in the treatment
and management of OSA in children.

The major citing articles in cluster #5 “Childhood obesity and OSA” were authored by
Arens and Muzumdar [115], with a coverage of 15 articles and a GCS of 138; Tauman and
Gozal [54], with a coverage of 14 articles and a GCS of 146; and Tauman and Gozal [116],
with a coverage of 14 articles and a GCS of 56. The main theme of the cluster appears to
be the occurrence of OSA with a focus on the population of children with obesity. This
is not surprising, due to research on this relation in obese adults as well as the surging
childhood obesity rates across the world. Notably, the occurrence of OSA seems to be
the prevalent clinical presentation in children with obesity [115] where some studies have
reported a prevalence of up to 45% in children with obesity [117]. The majority of citing
articles focus on obesity and OSA in children (e.g., [118–124]) including the major citing
articles mentioned above [54,115,116]. Similarly, the cited references are mainly studies
on the effects and clinical outcomes of children with OSA such as increased inflamma-
tion levels (e.g., [125–129]), negative cardiovascular consequences such as hypertension
(e.g., [130–134]) and metabolic consequences (e.g., [135,136]). Interestingly, in the cluster, Arens and Marcus [137] proposed a developmental perspective in framing the pathophysiology of upper airway obstruction which leads to OSA. In their developmental perspective, the authors consider that overall OSA is caused by a restriction in the anatomic airway and atypical upper airway neuromotor tone combined. On the one hand, as the authors argue, a reduction in the anatomic airway is typically observed independently from the age of the patient with OSA. On the other hand, upper airway neuromotor tone and reflexes during sleep vary throughout the lifespan and are superior in typical children as compared to adults to compensate for their smaller airway. It is noteworthy that upper airway neuromotor tone and reflexes during sleep are attenuated in children with OSA.

The major citing articles in cluster #4 “Pediatric obstructive sleep apnea” were authored by Kuo et al. [138], with a coverage of 14 articles and a GCS of 31; Bitners and Arens [139], with a coverage of 14 articles and a GCS of 21; and Gozal et al. [127], with a coverage of 13 articles and a GCS of 21. Cluster #4 appears to be a rapidly emerging cluster indicating the direction of attention towards the clinical presentation, treatment, and management of OSA in children as indicated by the citing articles [140–143] and cited references [62,119,144–146]. Particularly, Bitners and Arens [139] wrote a comprehensive review outlining the evaluation and management of children with complex medical comorbidities. In particular, the authors propose that all children should be screened for OSA and that referral to sleep expert or paediatric otolaryngologist and polysomnography, cardiology, and endocrinology evaluations should be conducted especially for those considered to be high-risk. In the cluster, there seems to be a number of studies concerned with the prognosis and post-operation outcomes relating to tonsillectomy and adenotonsillectomy in both the citing articles [147–149] and cited references [58,150,151], which is most likely due to the fact that adenotonsillectomy is one of the most commonly conducted surgical procedures in children for OSA treatment [152]. For example, the Children Adenotonsillectomy Trial (CHAT) [58] reported an overall success rate of 79% for surgery, although there was a lower likelihood for children with obesity, certain ethnicities, and more severe OSA. Results from CHAT have helped to inform evidence-based clinical practice guidelines [153], where notably, tonsillectomy is considered a first-line treatment for children with adenotonsillar hypertrophy.

4.7. Cluster #7: Cardiovascular Diseases and OSA

The major citing articles in cluster #7 were authored by Fava et al. [154], with a coverage of 35 articles and a GCS of 100; Gopalakrishnan and Tak [155], with a coverage of 21 articles and a GCS of 35; and Patrick et al. [156], with a coverage of 21 articles and a GCS of 50. Cluster #7 appears to be a niche cluster investigating the cardiovascular consequences and diseases associated with OSA. This is not surprising because sleep affects cardiovascular regulation and cardiovascular diseases are the leading cause of death across the world [157]. A way in which poor sleep quality and quantity influence cardiovascular regulation is by maintaining blood pressure at undesired stable levels during sleep and increasing, in turn, hypertension in sleep deprived populations. Particularly, in patients with OSA, clinicians typically observe sympathetic activation, oxidative stress, and systemic inflammation [156]. Most of the citing articles, including the major citing articles [154–156] focused on the relationship between OSA and cardiovascular diseases (e.g., [158–162]) as did the cited references (e.g., [17,163–168]). Although there have been many clinical studies on the link between OSA and cardiovascular disorders, the results across studies are in some cases inconsistent as highlighted by Fava et al. [154] and Gopalakrishnan and Tak [155]. This suggests the complexity of this association and the formation of a cluster of work delving into the clarification of this relationship. However, the culmination of all these clinical evidence on humans and animal models are beginning to solidify the association between OSA and increased risk for cardiovascular conditions including hypertension, stroke, cardiac arrhythmia, and heart failure, which is strongly supported by the common pathogenesis between the two conditions. As argued by Patrick et al. [156], although the
association between OSA and cardiovascular disorders becomes stronger, it is still to be clarified whether chronic cardiovascular consequences benefit from treating OSA.

4.8. Cluster #1: Metabolic Disorders and OSA

The major citing articles in cluster #1 were authored by Lurie [85], with a coverage of 39 articles and a GCS of 8; Lurie [169], with a coverage of 37 articles and a GCS of 30; and Patrick et al. [156], with a coverage of 30 articles and a GCS of 50. The main theme of cluster #1 appears to be the metabolic consequences and disorders associated with OSA, as indicated by the citing articles [85,169–174] and the cited references [8,160,175–177]. As suggested by clinical observations and corroborated by studies conducted with animal models, obesity, and sleep disturbances both represent a risk factor for negative metabolic outcomes [171,172]. In fact, OSA is typically associated with insulin resistance, glucose intolerance, and dyslipidemia. Moreover, there seems to be an association between OSA and metabolic disorders such as increased risk for diabetes, non-alcoholic fatty liver disease and metabolic syndrome. Because metabolic disorders themselves are a predictor of cardiovascular diseases, this may explain why there are a number of citing articles and cited references investigating either cardiovascular or metabolic diseases or even both (e.g., [85,160]), which is also suggested by the cluster’s relatively lower silhouette score. This cluster suggests that metabolic and cardiovascular outcomes are closely linked and studied together in the research of OSA, further highlighting the complexity of OSA and the directions of its relationships with other health conditions. Ultimately, as was the case for cluster #7 “Cardiovascular diseases and OSA”, although a significant number of studies are confirming the association between OSA and adverse metabolic consequences, it is still unknown whether patients with metabolic disorders can benefit from sleep-focused treatments [171,172].

4.9. Cluster #6: OSA during Pregnancy

The major citing articles in cluster #6 were authored by Dominguez et al. [178], with a coverage of 17 articles and a GCS of 17; Dominguez et al. [179], with a coverage of 17 articles and a GCS of 25; and Subramani et al. [180], with a coverage of 15 articles and GCS of 76. The main theme of cluster #6 is OSA during pregnancy, which can be observed from the citing articles [178,179,181–185] and the cited references [186–192]. Notably, the prevalence of OSA ranges from 15 to 20% in obese pregnant women [179]. From the literature, while pregnancy is associated with many risk factors for OSA (e.g., weight gain, gestational diabetes), pregnancy itself appears to be a vulnerable time window for the development and worsening of OSA [179]. In fact, physiological modifications to the upper airway during pregnancy play an important role in the development and worsening of OSA. However, pregnant women have often been under-recognised as a population at risk for breathing disturbances during sleep. Addressing this problem is crucial, as women with breathing disturbances during sleep have a higher risk of experiencing pregnancy complications and negative pregnancy outcomes. Furthermore, these women have higher risk for adverse medical outcomes (e.g., severe respiratory suppressions) and mortality even after delivery Dominguez et al. [178,179]. For example, Facco et al. [190] found an independent association between hypertensive disorders in pregnancy and OSA. Dominguez et al. [181] also outlined the cascading effects of intermittent hypoxia and endothelial dysfunction characteristic of OSA as mechanisms of this association. There are significant health implications for this association since hypertensive disorders of pregnancy are a major cause for maternal and neonatal morbidity [193,194], as well as increased lifetime risk for cardiovascular disease in mothers. In the cluster, the cited references also revolve around postoperative outcomes for OSA, as discussed in cluster #43. Postoperative outcomes for OSA are a pertinent concern during pregnancy in the context of the Caesarean procedure during delivery (e.g., [195–197]), as well as diabetes (e.g., [19,190,198,199]), another common condition during pregnancy. This is further reinforced by the finding that pregnant women with OSA have a higher risk of requiring a Caesarean delivery and the association between
OSA and perinatal outcomes such as neonatal intensive care [189]. In terms of treatment, as for the general population, continuous positive airway pressure is the recommended approach in pregnant women with OSA [178]. However, it is worth noting that only a limited number of studies with small sample sizes have investigated the effect of continuous positive airway pressure in pregnant women with OSA [178].

4.10. Cluster #3: Epidemiology of OSA

The major citing articles in cluster #3 were authored by Lee and Sundar [200], with a coverage of 16 articles and a GCS of 13; Ogilvie and Patel [201], with a coverage of 12 articles and a GCS of 37; and Mattina and Calzolari [202], with a coverage of 11 articles and a GCS of 0. The main theme of cluster #3 appears to be the epidemiology of OSA, where most of the citing articles are focused on investigating the prevalence of OSA across populations with various clinical health conditions [201,203–208], demonstrating continued research attention directed towards populations that are at risk of OSA. Most of these studies demonstrate the high prevalence of OSA in at-risk populations, such as those with diabetes (e.g., [201,204]). In line with this notion, the cited references were often screening tools for sleep-disordered breathing or OSA (e.g., [51,63,209,210]) as well as past work examining the prevalence of OSA across populations [4,10,50,211] and risk for adverse health events in those with OSA [212–214]. For example, findings from the Wisconsin Sleep Study Cohort [50] for the 2007–2010 period indicate prevalence estimates of 10–17% of moderate to severe sleep-disordered breathing in men between 30 and to 70 years old and a prevalence of 3–9% in women in the same age range, representing a substantial increase in the last two decades alone. The population-based HypnoLaus study conducted in Switzerland in the 2009–2013 period indicate prevalence estimates of moderate–severe sleep disordered breathing in 49.7% in men and 23.4% in women aged 40 to 85 years old [4]. These variations in reported prevalence estimates are highlighted by Senaratna et al. [10], where the authors point towards significant heterogeneity in methodology and highlight the need for greater consensus in methodology and diagnostic criteria to facilitate cross-regional and cross-country comparisons with greater validity. The systematic review by Senaratna et al. [10] also suggests a continuum of OSA in the general population of varying severity, where higher AHI scores are less prevalent. In terms of adverse health outcomes, findings from the Sleep Heart Health Study [212] demonstrate a strong association between ischaemic stroke and OSA while Nagayoshi et al. [213] found greater risk of incident diabetes associated with severe OSA based on the analysis of data from the Sleep Heart Health Study and the Atherosclerosis Risk in Communities Study.

4.11. Cluster #20: Obesity Hypoventilation Syndrome

The major citing articles in cluster #20 were authored by Piper [215], with a coverage of 8 articles and a GCS of 0; Kakazu et al. [216], with a coverage of 7 articles and a GCS of 9; and Masa et al. [217], with a coverage of 6 articles and a GCS of 25. Cluster #20 has a clear focus on obesity hypoventilation syndrome, which refers to the combination of obesity, sleep disordered breathing, and chronic daytime hypercapnia, the abnormal increase in the blood carbon dioxide levels [216]. The citing articles mainly focus on obesity hypoventilation syndrome [215–218], as do the cited references [55,219–223]. Compared to other sleep disordered breathing disorders, i.e., overlap syndrome and OSA, findings from Lacedonia et al. [219] indicate that obesity hypoventilation syndrome has the highest prevalence of cardiovascular and metabolic comorbidities (e.g., diabetes mellitus) and mortality rates given its combination of obesity, high oxidative stress, chronic inflammation, poor sleep quality, and gas exchange. With increasing obesity rates across the globe, the frequent comorbidity of obesity hypoventilation syndrome and OSA, and the mortality associated with both conditions, it is encouraging that there is emerging research interest on obesity hypoventilation syndrome to address the lack of knowledge on the topic [222]. This recent research trends are encouraging, especially because obesity hypoventilation syndrome is often undiagnosed or misdiagnosed [215]. As a result, people with obesity
hypoventilation syndrome are frequently hospitalised and tend to report a poor quality of life. In terms of treatment, Piper [215] suggests a shift away from treatment centred around hypoventilation. In fact, treating these patients by means of continuous positive airway pressure appears to have limited effectiveness as it addresses only sleep disordered breathing and awake hypercapnia [224]. Notably, even with the administration of continuous positive airway pressure, cardiovascular outcomes in this syndrome do not seem to show significant improvements. This observation reinforces the notion that long-term treatment and management of obesity hypoventilation syndrome should not only focus on addressing hypoventilation symptoms, but that tackling obesity is also of paramount importance in terms of disease management [224].

4.12. Cluster #23: Biological Markers of OSA

The major citing articles in cluster #23 were authored by Chen et al. [225], with a coverage of 5 articles and a GCS of 2; Wang et al. [226], with a coverage of 4 articles and a GCS of 0; and Guscoth et al. [227], with a coverage of 3 articles and a GCS of 2. Cluster #23 appears to be an emerging cluster focused on identifying biological markers of OSA. The identification of biomarkers of OSA is important as it aims to overcome some limitations that are inherent in the traditional OSA screening instruments. Specifically, while polysomnography is the gold standard for OSA diagnosis, it remains quite inaccessible for many patients with suspect OSA. In fact, polysomnography has the disadvantage of being quite expensive, time-consuming, and uncomfortable for patients [225]. Similarly, the validity of traditional questionnaires for OSA screening when used in different populations is still not well established. This attention on tackling the embedded shortcomings of traditional instruments can be observed from how the cited references of this cluster examined diagnostic tools for OSA [63,228,229]. For example, Chiu et al. [228] conducted a meta-analysis on existing scales (e.g., Berlin Questionnaire, STOP-BANG, STOP, and the Epworth Sleepiness Scale) to assess their diagnostic accuracy. Their findings recommended the use of STOP-BANG, although there were varying degrees of sensitivity and specificity across OSA of different severity. To address the problem of instruments validity and accessibility, the citing articles also investigated various other markers (e.g., serum lipid profiles [227]) and techniques for the diagnosis of OSA. For instance, Chen et al. [225] attempted to develop a nomogram based on a series of predictors of OSA in bariatric surgery candidates (i.e., gender, habitual snoring, type 2 diabetes mellitus, neck circumference, body mass index, and age). With this nomogram, a good classification accuracy was obtained for the training and validation cohort, proving the clinical usefulness of the developed instrument. In a similar vein, other citing articles investigated portable sleep monitor testing [230] and skeletal muscle lipid content [231].

5. Conclusions

The current study made use of scientometrics to review the literature on OSA and obesity in a data-driven fashion. The review identified the article written by Peppard et al. [50] as the most impactful document in the data sample, as well as 13 main thematic domains in the OSA and obesity literature. Based on the thematic clusters, the role of medical imaging was highlighted in the initial comprehension of the pathophysiology and clinical manifestations of OSA and in supporting the diagnosis of the condition. Clinical implications and medical consequences of OSA were the key areas of interest in the literature, as evidenced from the sizeable clusters, largely focusing on increased cardiovascular and metabolic risk. Importantly, the epidemiology of OSA, which is often under-recognised and misdiagnosed especially in at-risk populations (e.g., pregnant women, obese children), is another research area highlighted by the cluster analysis. More recently, there is a trend toward research investigating the biomarkers of OSA as possible tools for diagnosis [225].

However, the analysis also highlighted the lack of a systematic approach in comparing the benefits of different treatments (e.g., mandibular advancement devices, hypoglossal pacemaker, and myofunctional therapy) and treatment outcomes in terms of cardiovascular-
lar and metabolic conditions in the existing literature. Moreover, the reviewed literature suggests that scarce research has evaluated the efficacy of patient-tailored treatment in OSA, especially for populations at risk. Specifically, the development of evidence-based screening and treatment for at-risk populations such as children and pregnant women was highlighted by the clusters, as well as the need for larger sample sizes in clinical trials to establish stronger evidence-based recommendations. Evidently, there are many medical fields involved in the diagnosis and treatment of OSA, from respiratory medicine, otorhinolaryngology, cardiology, pulmonology, anaesthesiology, endocrinology to immunology. These fields would all benefit from research that continues to investigate evidence-based assessments and treatments for OSA especially for underinvestigated populations (e.g., investigation of OSA in children with neurodevelopmental disorders and in developing countries) or populations at risk (e.g., pregnant women), including diagnostic tools for early identification for those at risk.

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Abbreviations
The following abbreviations are used in this manuscript:
OSA Obstructive Sleep Apnea
AHI Apnea–Hypopnea Index
DCA Document Co-Citation Analysis
LLR Log-Likelihood Ratio
GCS Global Citing Score
STOP Snoring, Tiredness during daytime, Observed apnea, and high blood Pressure
CHAT Children Adenotonsillectomy Trial

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