



## Review Article

# Nocturnal dialysis improves sleep apnea more than daytime dialysis: a meta-analysis of crossover studies



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## ABSTRACT

**Purpose:** To systematically review the literature for articles evaluating differences in polysomnography (PSG) data when patients are on primarily daytime hemodialysis (conventional hemodialysis or continuous ambulatory peritoneal dialysis) versus nocturnal hemodialysis (nocturnal hemodialysis or nocturnal peritoneal dialysis). Then to perform a meta-analysis on the available PSG data, specifically evaluating differences in apnea hypopnea index (AHI) and mean saturation of oxygen (SpO<sub>2</sub>) between these two groups.

**Methods:** Two authors systematically searched MEDLINE/Pubmed, Scopus, EMBASE, CINAHL, and Cochrane. Searches were performed through December 6, 2018.

**Results:** A total of four adult crossover studies (91 patients, age 50.4 ± 12.4, BMI 25.1 ± 5.3) reported PSG data. The daytime hemodialysis (DHD) and nocturnal hemodialysis (NHD) AHI decreased from 24.6 ± 18.2 to 12.6 ± 11.8 (events/hour) with a mean difference of -11.9 [95% CI -13.47, -10.37], Z score of 15.07 (P < 0.00001). The standardized mean difference was -1.35 [95% CI -2.70, 0.01]. Two studies reported mean SpO<sub>2</sub> changes during PSG. The DHD and NHD SpO<sub>2</sub> increased from 92.7 ± 2.4 to 94.7 ± 2.2 with a mean difference of 2.26 [95% CI -0.18, 4.71], Z score 1.82 (P = 0.07).

**Conclusion:** In the current literature, nocturnal hemodialysis improves AHI more than daytime hemodialysis. A trend towards improvement in mean SpO<sub>2</sub> with nocturnal dialysis was noted, but did not reach statistical significance. Consideration can be given for transitioning patients who have end stage renal disease and sleep apnea from daytime to nocturnal hemodialysis as an adjunct to other treatment modalities.

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## 1. Introduction

Sleep apnea is common in patients with end-stage renal disease (ESRD) and is up to 10 times more prevalent than in the general population [1–4]. Patients with ESRD have been observed to have a significantly increased number of both central and obstructive events on polysomnography (PSG) suggesting there is increased instability of central respiratory control and/or upper airway involvement associated with this disease process [5–7]. This is

often manifested clinically with the majority of ESRD patients reporting excessive daytime sleepiness [8,9].

ESRD patients who undergo conventional hemodialysis (CHD) have not shown improvement in their sleep apnea [7,10]. However, nocturnal hemodialysis (NHD) in these patients has shown improvement in their sleep apnea [10–12]. The exact cause of improvement in sleep apnea in ESRD patients undergoing NHD is not completely understood, however, multiple mechanisms have been proposed: increased clearance of uremic toxins [13,14], improved ultrafiltration [15] with increased clearance of extracellular fluid [16], and the association of uremia with altered neural responsiveness of upper airway muscles in ESRD [17].

Additionally, several studies have shown a correlation between upper airway edema and sleep apnea [18–20]. Lower body trousers placed on healthy non obese patients to displace fluid from the lower extremities to the upper body have been shown to increase

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pharyngeal airflow resistance [21]. Leg raising in healthy subjects has also shown increased upper airway resistance [21,22]. Diuretic therapy in patients with heart failure has shown to increase pharyngeal cross sectional area and a decrease in apnea hypopnea index (AHI) [23]. Prior research has shown an association of ESRD with narrowing of pharyngeal cross-sectional area [24]. These studies have postulated that worsening of sleep apnea in volume overloaded states occurs through increased rostral fluid shift and decreases in pharyngeal cross-sectional area.

The objective of this study was to systematically review the literature for articles evaluating differences in PSG data when ESRD patients are on primarily daytime hemodialysis versus nocturnal hemodialysis. Then, the next step was to perform a meta-analysis on the available PSG data.

## 2. Methods

### 2.1. Search strategy

Two authors (MRL and JAP) independently performed the search on Pubmed, Scopus, EMBASE, CINAHL, and Cochrane from April 17th, 2017 to March 19th, 2018. Keywords used for the search included: “fluid shift”, “dialysis”, “hemodialysis”, “sleep disordered breathing”, “oxygen desaturation”, “sleep apnea”, and “sleep apnoea”. One example of a PubMed search is (“fluid shift”) AND (“dialysis” OR “hemodialysis” OR “sleep disordered breathing” OR “oxygen desaturation” OR “sleep apnea” OR “sleep apnoea”).

When searching each database, titles and abstracts were screened and full text versions of articles that met criteria were downloaded. Full texts and their references were reviewed, any article not obtained was requested through the institutional inter-library loan. “Related citations” within each studies were also reviewed to gather additional studies.

### 2.2. Study selection

Studies were included with no limitation placed on year of publication, country, or language. The inclusion criteria for the studies followed the PICOS acronym [1]: Patients: any adult patient

(≥18 years old) on dialysis with data for controls; [2] Intervention: nocturnal hemodialysis; [3] Comparison: results from day time dialysis [4]; Outcomes: any quantitative data, studies needed to report quantitative PSG data pre-treatment and post-treatment and [5]; Study design: any study design from case reports through randomized controlled-trials. Exclusion criteria: studies in children, studies in patients with concomitant heart failure and studies without quantitative data.

### 2.3. Data abstraction and study quality assessment

After independently searching international literature, screening titles and abstracts and downloading articles to review, a consensus between two authors (MRL and JAP) was reached on which articles to include and if necessary the final decision was to be made by author MC. Data collected include patient age, body mass index (BMI), and PSG data (AHI, mean SpO<sub>2</sub>). If data were missing from the article then the corresponding author was contacted in an attempt to obtain this data. The corresponding author of the article Hanly 2003 was contacted for mean SpO<sub>2</sub> data of patients who underwent nocturnal hemodialysis. Given the similarities in patient data in Beecroft 2008 and 2009, the corresponding author for these papers was contacted. This author confirmed significant overlap in the patient population of these two studies but did not have individual patient data available for comparison, thus the patients from the 2008 study were not included in our analysis. Additionally, after further review one article [11] added patient data from a prior study [25], thus the earlier study was excluded and the data from the newest article was used.

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were followed during this review and has been included in Fig. 1 [26]. The National Institute for Health and Clinical Excellence (NICE) quality assessment tool was used to evaluate the quality of the included studies.

### 2.4. Statistical analysis

Statistics were performed using multiple statistics software to include: (1) The Statistic Toolkit Website (StatsToDo) from the

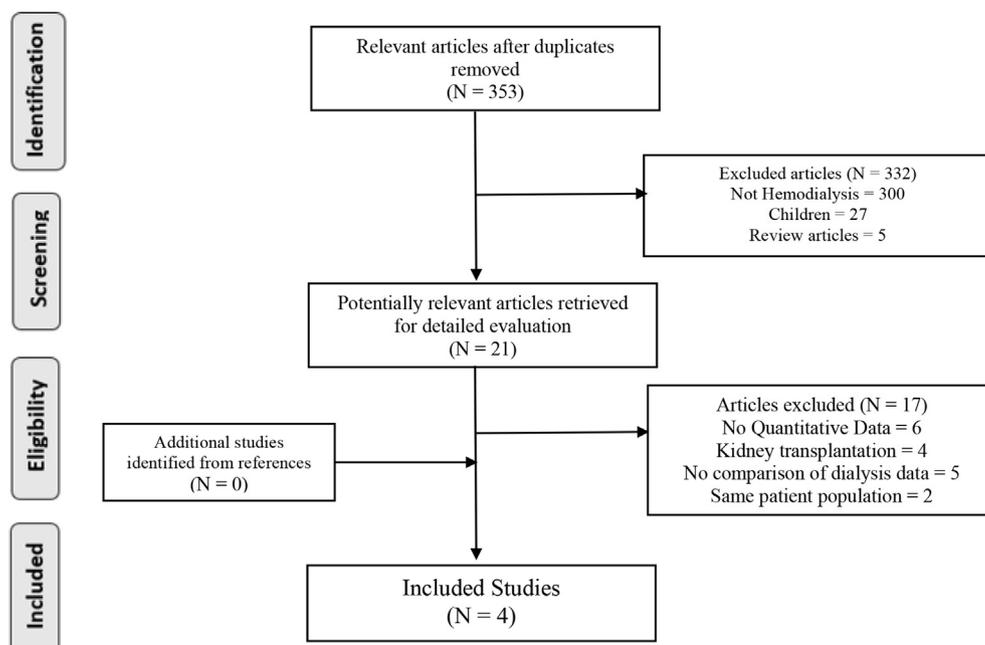
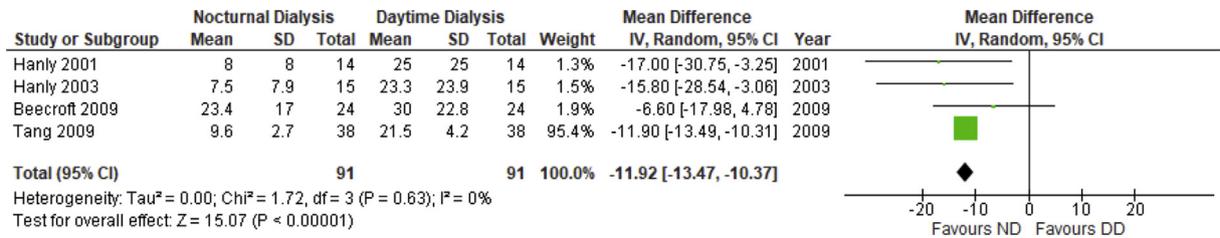


Fig. 1. Flow chart for study selection. (N: number of studies), Artwork created in Microsoft Word.



**Fig. 2.** Comparison of nocturnal and daytime dialysis for apnea hypopnea index (events per hour) outcomes. CI, confidence interval; DD, daytime dialysis (includes continuous ambulatory peritoneal dialysis and conventional hemodialysis); ND, nocturnal dialysis (includes nocturnal peritoneal dialysis and nocturnal hemodialysis); SD, standard deviation, Forest Plot Created in Review Manager (RevMan) [Computer program] Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Chinese University of Hong Kong and (2) Review Manager (RevMan) [Computer program] Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) were used for meta-analysis. Means and standard deviations were calculated on daytime hemodialysis and on nocturnal hemodialysis. The null hypothesis for this study is that there is no difference in outcome data for daytime hemodialysis vs nocturnal hemodialysis. For combining data a two-tailed, paired t-test was performed ( $P < 0.05$  was the cutoff for significance). A random effects model was used. Data in the studies were collated and the means, standard deviations, and 95% confidence intervals (CI) were calculated by RevMan. Heterogeneity was assessed by I<sup>2</sup> statistic (inconsistency levels: low = 25%, moderate = 50% and high = 75%) [27].

### 3. Results

A total of 353 articles were screened and 332 were excluded. 21 potentially relevant articles were downloaded in full text for review and 4 studies met full criteria. All crossover studies reported outcomes with means and standard deviations and were used for this meta-analysis [10–12,28]. Fig. 1 summarizes the flow for study selection.

#### 3.1. Methodological quality of the included studies

The studies included in this meta-analysis were four crossover studies [10–12,28]. All studies fulfilled at least 5/8 NICE quality assessment tool items. The main limitations of the studies were that they were not multi-centered, had small sample sizes, and they did not explicitly state that patients were recruited consecutively.

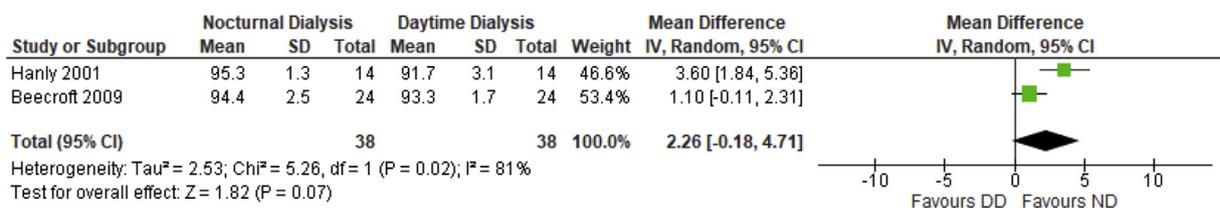
##### 3.1.1. Hanly 2001

This study enrolled 14 ESRD patients who were not assessed for previous sleep disordered breathing and were already undergoing conventional hemodialysis (CHD, three sessions per week, 4 h each session). Patients underwent one PSG and biochemical analysis on the night of CHD, and one two days after their last session of CHD.

Then, the same patients were transitioned to six weeks of nocturnal hemodialysis (NHD, six days per week with 8 h per session). After these six weeks, patients underwent a PSG on a night of NHD, and another on a night when patients were off NHD. There was a statistically significant decrease in AHI when patients were switched from CHD to NHD [AHI events/h:  $25.0 \pm 25.0$  to  $8.0 \pm 8.0$ ; Mean difference  $-17.00$  events/h (95% CI  $-30.75, -3.25$ )] (Fig. 2). It was also noted that when patients were on NHD, their AHI on nights when they did not receive NHD trended towards being higher as compared to the nights when they were on NHD. The authors also noted significant improvement in oxygen saturation and less respiratory arousals in these patients when they were on NHD vs CHD [Mean SpO<sub>2</sub>:  $91.7 \pm 3.1$  vs.  $95.3 \pm 1.3$ ; Mean difference 3.6 (95% CI 1.84, 5.36)] (Fig. 3). For our calculation of BMI in the NICE table, the BMI means reported were statistically combined using the statistical software. The AHI and SpO<sub>2</sub> means were included from the means of “Day of CHD” and “day on NHD” data.

##### 3.1.2. Hanly 2003

In this study, 24 patients already on CHD (three days per week, 4 h per day) and not previously assessed for sleep disordered breathing were enrolled. A PSG was conducted on the night after CHD, and another conducted two days after last CHD session. 15/24 patients underwent transition to nocturnal hemodialysis and the other nine patients elected to not undergo transition. The transition consisted of patient training for six weeks. Once fully transitioned, the patients returned to the sleep lab and PSG was conducted while the patients were on nocturnal hemodialysis. Additionally, another PSG was conducted on one single night when patients were taken off of NHD. AHI significantly improved in these patients when they were transition to NHD from CHD [AHI events/h:  $23.3 \pm 23.9$  to  $7.5 \pm 7.9$ ; mean difference  $-15.80$  (95% CI  $-28.54, -3.06$ )] (Fig. 2). We reconstituted the study data to calculate the overall mean data for the 15 patients who underwent NHD. Mean age, BMIs and changes in mean SpO<sub>2</sub> were not reported for the group of 15 patients that transitioned to NHD (data was only presented for all 24 patients together). The corresponding author was contacted by email for this additional data but was unable to be reached. The AHI



**Fig. 3.** Comparison of nocturnal and daytime dialysis for oxygen saturation (percent). CI, confidence interval; DD, daytime dialysis (includes continuous ambulatory peritoneal dialysis and conventional hemodialysis); ND, nocturnal dialysis (includes nocturnal peritoneal dialysis and nocturnal hemodialysis); SD, standard deviation, Forest Plot Created in Review Manager (RevMan) [Computer program] Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

data used in Table 1 was from the data set “on day 0 of CHD” and “on NHD”.

### 3.1.3. Beecroft 2009

This group enrolled 24 ESRD patients already on CHD. Baseline studies to include PSG and chemoreflex responsiveness were performed within 24 h of last CHD session. Patients then underwent 5–6 weeks of home NHD training and were brought for follow up studies once using NHD (6–10 h per night, 3–6 nights per week) without issue, usually about 3–6 months later. Follow up studies were performed on a night the patients were not receiving dialysis. Chemoreflex responsiveness testing was conducted while patients were awake during episodes of hypoxia and hyperoxia. Data was again split into two groups based on AHI of 15 or greater (apneic) or less (non-apneic). This study did not report a statistically significant improvement on AHI when on NHD from CHD [AHI events/h:  $30.0 \pm 22.8$  to  $23.4 \pm 17.0$ ; mean difference  $-6.60$  (95% CI  $-17.98$ ,  $4.78$ )] (Fig. 2). Mean SpO<sub>2</sub> data was reported but was not statistically significant [Mean SpO<sub>2</sub>:  $93.3 \pm 1.7$  vs.  $94.4 \pm 2.5$ ; Mean difference 1.1 (95% CI  $-0.11$ ,  $2.31$ )] (Fig. 3). AHI and ventilatory sensitivity were positively correlated in both hypoxic and hyperoxic conditions in apneic patients. When all patients were analyzed, ventilatory sensitivity was not significantly different in CHD vs NHD groups. There was a positive correlation on comparison of AHI and ventilator sensitivity when converted to NHD during hyperoxia, but not during hypoxia. Our mean age and BMI data were calculated via combining means in statistical software. AHI and SpO<sub>2</sub> means were calculated by using apneic and non-apneic data and combining means in statistical software.

### 3.1.4. Tang 2009

This study recruited individuals during a temporary period of cyclor assisted nocturnal peritoneal dialysis (NPD) for approximately eight weeks, after which they were converted to continuous ambulatory peritoneal dialysis (CAPD). One PSG was conducted near the end of 6–8 weeks of NPD and a second PSG was conducted after established on stable CAPD. The study used data on 24 incident CAPD patients [25] and another 14 new patients were recruited and added to this study. This study reports PSG data for 38 patients, body water composition via bioelectrical impedance analysis for 29, and MRI data for 14. Patients underwent MRI scan of their upper airway when awake within 6 h of completing NPD or in the night while on CAPD. AHI values increased significantly when patients were converted to CAPD from NPD [AHI events/h:  $21.5 \pm 4.2$  to  $9.6 \pm 2.7$ ; mean difference  $-11.90$  (95% CI  $-13.49$ ,  $-10.31$ )] (Fig. 2). Mean SpO<sub>2</sub> data was not reported. NPD was associated with greater fluid removal (significant reductions in absolute body water contents). The patients that did undergo MRI during NPD and CAPD showed significant reduction of aggregate airway volumes, minimal cross sectional area, and increased tongue volumes when switching from NPD to CAPD. This study also noted improvement in central apneic events when patients were

on NPD. BMI for our table was taken from the “On NHD” data set as patients in this study started on NHD.

## 3.2. Studies

A total of four adult crossover studies (91 patients, age  $50.4 \pm 12.4$ , BMI  $25.1 \pm 5.3$ ) reported PSG data. The daytime hemodialysis (DHD) and nocturnal hemodialysis (NHD) AHI decreased from  $24.6 \pm 18.2$  to  $12.6 \pm 11.8$  (events/hour) with a mean difference of  $-11.9$  [95% CI  $-13.47$ ,  $-10.37$ ], Z score of 15.07 ( $P < 0.00001$ ) (Table 1 and Fig. 2), and the I<sup>2</sup> statistic was 0% indicating minimal heterogeneity. The standardized mean difference was  $-1.35$  [95% CI  $-2.70$ ,  $0.01$ ]. On exclusion of the Tang et al. article [11], the only study using peritoneal dialysis, the mean difference was  $12.43$  [95% CI  $-19.65$ ,  $-5.2$ ], Z score 3.37 ( $P = 0.0007$ ), I<sup>2</sup> = 0%. The standard mean difference was  $-0.61$  [95% CI  $-1.01$ ,  $-0.22$ ].

Of these studies, two additionally reported mean SpO<sub>2</sub> changes during PSG (Table 1). The DHD and NHD SpO<sub>2</sub> increased from  $92.7 \pm 2.4$  to  $94.7 \pm 2.2$  with a mean difference of 2.26 [95% CI  $-0.18$ ,  $4.71$ ], Z score 1.82 ( $P = 0.07$ ) and I<sup>2</sup> statistic of 81% indicating significant heterogeneity. Tang et al., did not report mean SpO<sub>2</sub> data during PSG but did note that after switching to CAPD from NPD the duration of sleep with oxygen saturation  $<90\%$  was significantly higher ( $P = 0.025$ ) [11].

## 4. Discussion

This systematic review and meta-analysis of four adult studies evaluating the effect of nocturnal hemodialysis on sleep apnea has two main findings. First, nocturnal dialysis results in reduction of AHI. When comparing DD and ND, AHI decreased from  $24.6 \pm 18.2$  (DD) to  $12.6 \pm 11.8$  (ND) (events/h) with a mean difference of  $-11.9$  events/h [95% CI  $-13.47$ ,  $-10.37$ ], Z score of 15.07 ( $P < 0.00001$ ) (Fig. 2). There was evidence of central, obstructive, and mixed apneic events in these ESRD patients although obstructive apneic events tend to predominate. Second, when comparing mean SpO<sub>2</sub> between DD and ND, SpO<sub>2</sub> increased from  $92.7 \pm 2.4$  to  $94.7 \pm 2.2$  with a mean difference of 2.26 [95% CI  $-0.18$ ,  $4.71$ ] (Fig. 3).

As stated previously, there are several mechanisms that have been proposed to explain these observed findings. One theory is that central hypocapnia may be secondary to chronic metabolic acidosis in these patients which results in development of periodic breathing. Attenuation of metabolic acidosis will theoretically control hypocapnia and reverse suppression of the respiratory center resulting in diminished hypocapnia [7,29]. However, Tang et al., showed little change in bicarbonate between NPD and CAPD, suggesting this may not be a predominant mechanism for the observed outcome [11].

Other theories also exist. Beecroft et al., showed changes in chemoreflexive sensitivity associated with NHD [28]. Their previous study has shown increased ventilator sensitivity to hypercapnia

**Table 1**  
Adult nocturnal and daytime dialysis outcomes.

Authors, year	Study design	N	Age (years)	BMI (kg/m <sup>2</sup> )	AHI (events/hr)		Mean SaO <sub>2</sub>	
					DD	ND	DD	ND
Hanly et al., 2001	Crossover	14	$45.0 \pm 9.0$	$25.7 \pm 4.8$	$25.0 \pm 25.0$	$8.0 \pm 8.0$	$91.7 \pm 3.1$	$95.3 \pm 1.3$
Hanly et al., 2003	Crossover	15	—	—	$23.3 \pm 23.9$	$7.5 \pm 7.9$	—	—
Beecroft et al., 2009	Crossover	24	$47.5 \pm 10.8$	$27.9 \pm 6.7$	$30.0 \pm 22.8$	$23.4 \pm 17.0$	$93.3 \pm 1.7$	$94.4 \pm 2.5$
Tang et al., 2009	Crossover	38	$54.2 \pm 13.3$	$23.2 \pm 3.6$	$21.5 \pm 4.2$	$9.6 \pm 2.7$	—	—
Total		91	$50.4 \pm 12.4$	$25.1 \pm 5.3$	$24.6 \pm 18.2$	$12.6 \pm 11.8$	$92.7 \pm 2.4$	$94.7 \pm 2.2$

AHI, apnea hypopnea index; BMI, body mass index; DD, daytime dialysis (includes continuous ambulatory peritoneal dialysis and conventional hemodialysis); N, number of patients in the study; ND, nocturnal dialysis (includes nocturnal peritoneal dialysis and nocturnal hemodialysis), SaO<sub>2</sub>, arterial oxygen saturation (the studies reported SaO<sub>2</sub> but used SpO<sub>2</sub> as surrogate marker).

in ESRD [30]. This may precipitate alterations in chemoreflexive responsiveness with development of cycles of hypercapnia and hypocapnia. As a patient's systemic CO<sub>2</sub> builds up during apnea, this could potentially stimulate increased ventilation, which may be excessive resulting in hypocapnia and hypoventilation allowing subsequent apnea [31], and thus continuing the cycle. Periodic breathing may also increase upper airway obstruction due to reduction of signal to upper airway musculature [32,33]. A resumption of breathing from a central apneic event may be followed by an imbalance between inspiratory musculature and upper airway dilators. Patients who are prone to OSA, by pharyngeal narrowing for example, may have concomitant central respiratory instability as is likely true in patients with ESRD. NHD may help correct sleep apnea by stabilizing central chemoreflex sensitivity [31] and thus lessening the effects of concomitant OSA.

ESRD patients may be more susceptible to development of OSA (with or without central sleep apnea) due to their fluid overload state resulting in potential rostral fluid shifts overnight. This may result in increased airway edema with concomitant decrease in upper airway cross-sectional area. Increased fluid removal during the night may result in decreased rostral fluid shift with simultaneous improvement in OSA. NHD has been shown to decrease extracellular fluid volume previously [34]. Tang et al., reported NPD had greater fluid removal than CAPD with significant reductions in absolute body water contents (total body water 2.2× reduction ( $P = 0.003$ ) and extracellular body water 1.9× reduction ( $P = 0.005$ )) [11]. ND provides continued fluid removal throughout the night whereas DD may allow fluid accumulation overnight, resulting in increased airway edema and resistance, thus possibly promoting or worsening sleep apnea. Tang et al., also reported significant reductions in nasopharyngeal ( $-24.5 \pm 9.6\%$ ), oropharyngeal volumes ( $-34.0 \pm 11.6\%$ ), and minimal cross sectional pharyngeal area ( $-16.8 \pm 4.7\%$ ) when switched from NPD to CAPD [11]. This was analyzed by volumetric MRI [35]. This change in upper airway structure may worsen OSA or lead to OSA in those patients with predisposing risk factors. Conversely, Beecroft et al., reported the change in pharyngeal cross sectional area (as measured by acoustic pharyngometry) was not associated with a change in AHI suggesting increased pharyngeal cross sectional area alone may not be accountable for improvement in sleep apnea by NHD [36].

Of note, obstructive apnea may increase the likelihood of developing central apneic events. Periodic breathing is more likely to develop in patients with chronic renal failure than unaffected individuals, potentially secondary to airway edema and decreased upper airway muscle tone [32,37]. Narrowing of the upper airway has been linked to induction of sleep apnea [38]. Tang et al., reported four patients without a history of heart failure or stroke that developed new Cheyne-Stokes breathing after switching from NPD to CAPD, suggesting increased fluid may have contributed to the development of this central apnea syndrome [25].

Also of note, Beecroft et al. [28] were the only study in this meta-analysis that did not report overall statistically significant improvement in AHI on conversion from CHD to NHD. However, they reported a sub-group of apneic patients (responders) who had improvement in their AHI after conversion from CHD to NHD. Another limitation of this study included the rating of apneic patients based on AHI greater than 15 events/h. Currently, severity of sleep apnea is divided into three categories of mild (AHI 5–15 events/h), moderate (AHI 15–30 events/h), and severe (AHI > 30 events/h). Therefore, we suspect the number of responders would change if the statistical analysis were to be redone based on current definitions of OSA. This study also differed from the others as the NHD schedule was only 3–6 nights per week

(versus 6 nights per week in other studies) and PSG was conducted on a night when the patient was not undergoing NHD, thus potentially allowing increased rostral fluid shifting or accumulation of other mediators during that period. All of the other studies we reported conducted a PSG on the night of NHD.

Moreover, it is noteworthy that in all reported studies there was no prior evaluation of sleep apnea in these patients. Thus, many patients that did not respond with as significant an AHI reduction may have had previously undiagnosed sleep apnea or had developed some upper airway abnormality independently of ESRD. NHD is unlikely to improve sleep apnea that is independent of ESRD.

In terms of oxygen saturation, SpO<sub>2</sub> trended towards significance with nocturnal dialysis but did not reach statistical significance likely due to the small sample size ( $n = 38$ ). Nocturnal hypoxemia in dialysis patients has been linked to significant cardiovascular complications [39]; therefore, further research may help confirm if there is truly a significant improvement with nocturnal dialysis and subsequently improved, clinically significant cardiovascular outcomes.

There are several directions for future studies. Several articles we analyzed reported relatively low flow NHD to avoid adverse consequences during the night. Further investigation could explore what is the optimal amount of NHD to improve sleep apnea. Additionally, future studies can explore the role of less well recognized potential contributors to sleep apnea such as middle molecules. CHD has been associated with accumulation of middle molecules, which may have an effect on sleep apnea but have not been investigated, and NHD may reverse accumulation of such molecules [40,41]. Lastly, further study on the effects of increased intraperitoneal pressure in peritoneal dialysis patients on AHI, arousals, and airway collapse may be considered.

#### 4.1. Limitations

There are only four studies with data for 91 patients to analyze AHI outcomes. Despite this relatively small number, there was significant improvement of AHI with nocturnal dialysis. Additionally, amongst these four studies, only two (38 patients) reported data for mean PSG SpO<sub>2</sub>. Although the data was not statistically significant, the trend was in the favor of nocturnal dialysis. More studies with larger number of patients are needed to validate statistical and clinical significance of this finding. The average patient follow up was 2–6 months in these studies. Currently, it is unclear if the benefit of nocturnal dialysis is sustained beyond this and longer follow up studies will be required to answer this question. Additionally, longer follow up may be able to identify if this reduction in AHI and possible improvement in nocturnal SpO<sub>2</sub> results in improved clinical outcomes. Also, as mentioned previously, all of the patients in these studies had not been evaluated for sleep apnea prior to enrollment. Thus, these patients may have had sleep apnea or had developed some upper airway abnormality independently of ESRD. Strict inclusion criteria and patient selection in future studies will help to investigate the role of ESRD in sleep apnea which may further improve outcomes and emphasize a more individualized approach to patient care. However, since most ESRD patients have multiple medical comorbidities, it will be difficult to mitigate the effect of confounding variables associated with sleep apnea in this patient population. Another limitation of our study is the risk of bias with our searching algorithm and study selection; alternately, our use of a comprehensive search and review strategy performed by two different authors independently limited this problem.

## 5. Conclusion

In the current literature, nocturnal hemodialysis has improved AHI more than daytime hemodialysis. The increase in mean SpO<sub>2</sub>, though not statistically significant, trended towards improvement. Consideration can be given for transitioning patients who have end stage renal disease and sleep apnea from daytime to nocturnal hemodialysis as an adjunct to other treatment modalities.

## Disclosure statement

The views expressed in this abstract/manuscript are those of the author(s) and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the US Government.

## Financial interests

No financial and no material support for this research and work.

## Disclosure of any off-label or investigational use

None.

## Ethical standards

Permission was obtained from Madigan Army Medical Center for this study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

## Conflicts of interest

The authors declare that they have no conflict of interest.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: <https://doi.org/10.1016/j.sleep.2019.06.005>.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sleep.2019.06.005>.

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