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Effect of Positive Airway Pressure Therapy on Mortality in European Obstructive Sleep Apnea Patients: Post Hoc Analysis of a Global Meta-Analysis

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INTRODUCTION

- **Obstructive Sleep Apnea (OSA)** is a prevalent sleep-related breathing disorder linked to increased **all-cause** and **cardiovascular (CV) mortality**. Positive Airway Pressure (PAP) therapy is the first-line treatment shown to improve sleep quality, reduce hypoxic burden, and stabilize cardiovascular function.
- While **observational studies** consistently show mortality benefits with PAP therapy, findings from **randomized controlled trials (RCTs)** have been mixed, creating uncertainty about its long-term survival impact. These discrepancies may be influenced by **study design, patient selection, adherence variability**, and **regional healthcare factors**.
- To better understand the impact of PAP in a more homogeneous setting, we conducted a **European-focused post hoc analysis** using data extracted from a recent global meta-analysis (*Benjafield et al., Lancet Respir Med, 2025*), evaluating PAP's effect on mortality outcomes specifically in European adults with OSA.

METHODS

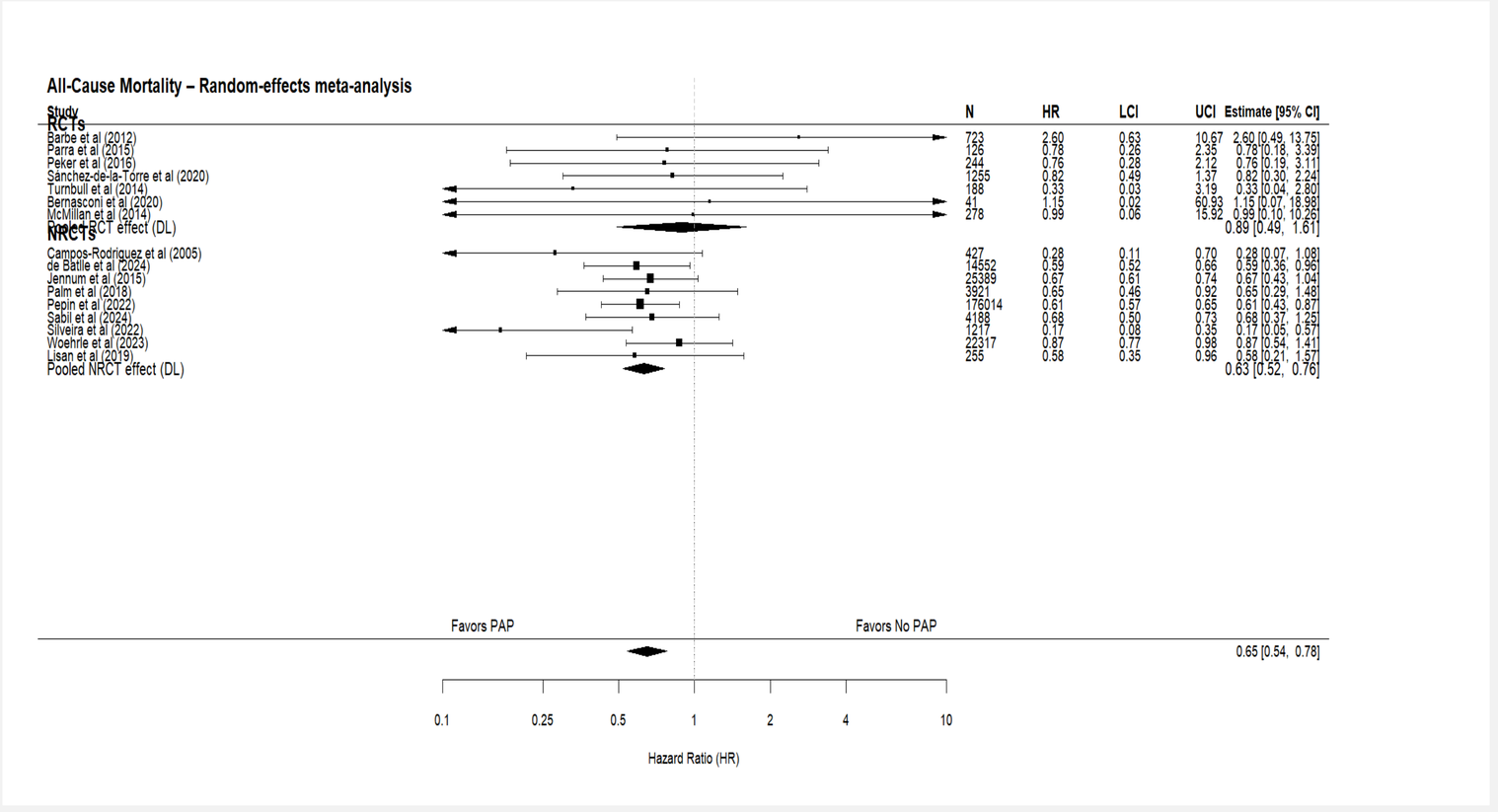
This post hoc subgroup analysis focused on **European studies** included in a recent global meta-analysis (*Benjafield et al., Lancet Respir Med, 2025*), assessing the impact of **positive airway pressure (PAP)** therapy on mortality outcomes in patients with **obstructive sleep apnea (OSA)**.

- **Data Source**: Published **hazard ratios (HRs)** and **95% confidence intervals (CIs)** were extracted directly from the original forest plots.
- **Sample Size**: Combined total of **254,205 patients**, across **randomised controlled trials (RCTs)** and **non-randomised controlled trials (NRCTs)**. NRCs in the original meta-analysis were adjusted for key confounders
- **Data Computation**: **Log(HR)** and **standard errors (SEs)** were calculated from the reported CIs, assuming a **log-normal distribution**
- **Models Used:**
  - DerSimonian-Laird (DL): Standard random-effects model.
  - Hartung-Knapp-Sidik-Jonkman (HKSJ): Conservative sensitivity model, adjusts for small sample sizes.
- **Stratification:** Randomized controlled trials (RCTs) , non-randomised controlled trials (NRCTs) and overll pooled.
- **Software: R (metafor).**

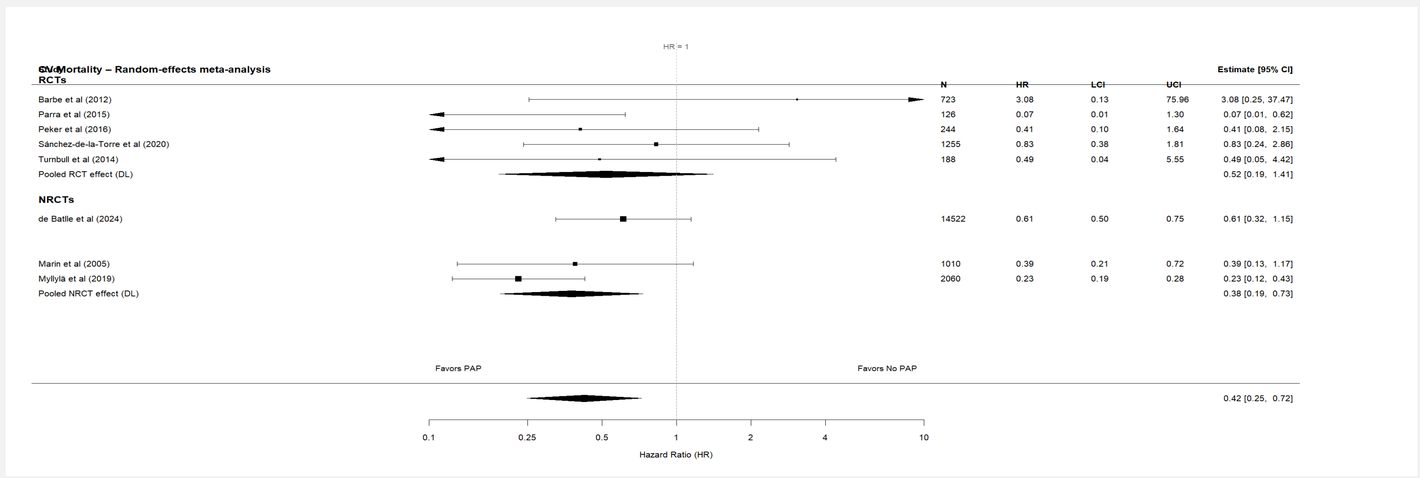
RESULTS

- Eighteen studies (n = 254,205) met inclusion criteria: 7 RCTs (n = 2,855) and 11 NRCs (n = 251,350).
- **For all-cause mortality** (RCT=7; NRCs=9), the DL model showed a significant overall benefit of PAP (HR = 0.65; 95% CI: 0.54-0.78), with stronger effects in NRCTs (HR = 0.63; 95% CI: 0.52-0.76), while effects in RCTs were not significant (HR = 0.89; 95% CI: 0.49-1.61). HKSJ results were similar (HR = 0.65; 95% CI: 0.55-0.77), with consistent patterns across study types.
- **For CV mortality** (RCT=5; NRCs=3), PAP therapy was linked to a significant overall reduction in risk in the DL model (HR = 0.42; 95% CI: 0.25-0.72), with strong effects in NRCTs (HR = 0.38; 95% CI: 0.19-0.73) and non-significant results in RCTs (HR = 0.52; 95% CI: 0.19-1.41). HKSJ estimates confirmed the findings with wider uncertainty (overall HR = 0.42; 95% CI: 0.22-0.81).

All cause mortality							
Study	**Study Type**	**Sample Size**	**HR**	**Lower CI**	**Upper CI**	**logHR**	**SE**
Barbe et al (2012)	RCT	723	2.6	0.63	10.67	0.96	0.72
Parra et al (2015)	RCT	126	0.78	0.26	2.35	-0.25	0.56
Peker et al (2016)	RCT	244	0.76	0.28	2.12	-0.27	0.52
SÃ¡nchez-de-la-Torre et al (2020)	RCT	1255	0.82	0.49	1.37	-0.20	0.26
Turnbull et al (2014)	RCT	188	0.33	0.03	3.19	-1.11	1.19
Bernasconi et al (2020)	RCT	41	1.15	0.02	60.93	0.14	2.05
McMillan et al (2014)	RCT	278	0.99	0.06	15.92	-0.01	1.42
Campos-Rodriguez et al (2005)	NRCT	427	0.28	0.11	0.7	-1.27	0.47
de Batlle et al (2024)	NRCT	14552	0.59	0.52	0.66	-0.53	0.06
Jennum et al (2015)	NRCT	25389	0.67	0.61	0.74	-0.40	0.05
Palm et al (2018)	NRCT	3921	0.65	0.46	0.92	-0.43	0.18
Pepin et al (2022)	NRCT	176014	0.61	0.57	0.65	-0.49	0.03
Sabil et al (2024)	NRCT	4188	0.68	0.5	0.73	-0.39	0.10
Silveira et al (2022)	NRCT	1217	0.17	0.08	0.35	-1.77	0.38
Woehrle et al (2023)	NRCT	22317	0.87	0.77	0.98	-0.14	0.06
Lisan et al (2019)	NRCT	255	0.58	0.35	0.96	-0.54	0.26



CV mortality							
Study	**Study Type**	**Sample Size**	**HR**	**Lower CI**	**Upper CI**	**logHR**	**SE**
Barbe et al (2012)	RCT	723	3.08	0.13	75.96	1.12493	1.62511
Parra et al (2015)	RCT	126	0.07	0	1.3	-2.6593	inf
Peker et al (2016)	RCT	244	0.41	0.1	1.64	-0.8916	0.71359
Sánchez-de-la-Torre et al (2020)	RCT	1255	0.83	0.38	1.81	-0.1863	0.39819
Turnbull et al (2014)	RCT	188	0.49	0.04	5.55	-0.7133	1.25834
de Batlle et al (2024)	NRCT	14522	0.61	0.5	0.75	-0.4943	0.10343
Marin et al (2005)	NRCT	1010	0.39	0.21	0.72	-0.9416	0.31432
Myllylä et al (2019)	NRCT	2060	0.23	0.19	0.28	-1.4697	0.09892



CONCLUSION

PAP therapy significantly reduces all-cause and cardiovascular mortality among European adults with OSA. The effect is most pronounced in adjusted non-randomised studies, underscoring its real-world survival benefits. These findings reinforce PAP as a life-saving intervention and highlight the urgent need for broader access and adherence support across Europe.

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