Obstructive Sleep Apnea and Commercial Motor Vehicle Driver Safety

Findings of Evidence Report

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Key Questions

- Key Question 1: Are individuals with obstructive sleep apnea (OSA) at an increased risk for a motor vehicle crash when compared to comparable individuals who do not have OSA?
- Key Question 2: What disease-related factors are associated with an increased motor vehicle crash risk among individuals with OSA?
- Key Question 3: Given the findings of Key Question 2, are individuals with OSA unaware of the presence of the factors that appear to be associated with an increased motor vehicle crash risk?

Key Questions

- Key Question 4: Are there screening/diagnostic tests available that will enable examiners to identify those individuals with OSA who are at an increased risk for a motor vehicle crash?
- Key Question 5: Which treatments have been shown to effectively reduce crash risk among individuals with OSA?
- Key Question 6: What is the length of time required following initiation of an effective treatment for individuals with OSA to reach a degree of improvement that would permit safe driving?

Key Questions

- Key Question 7: How soon, following cessation of treatment (i.e., as a consequence of non-compliance), will individuals with OSA demonstrate reduced driver safety?

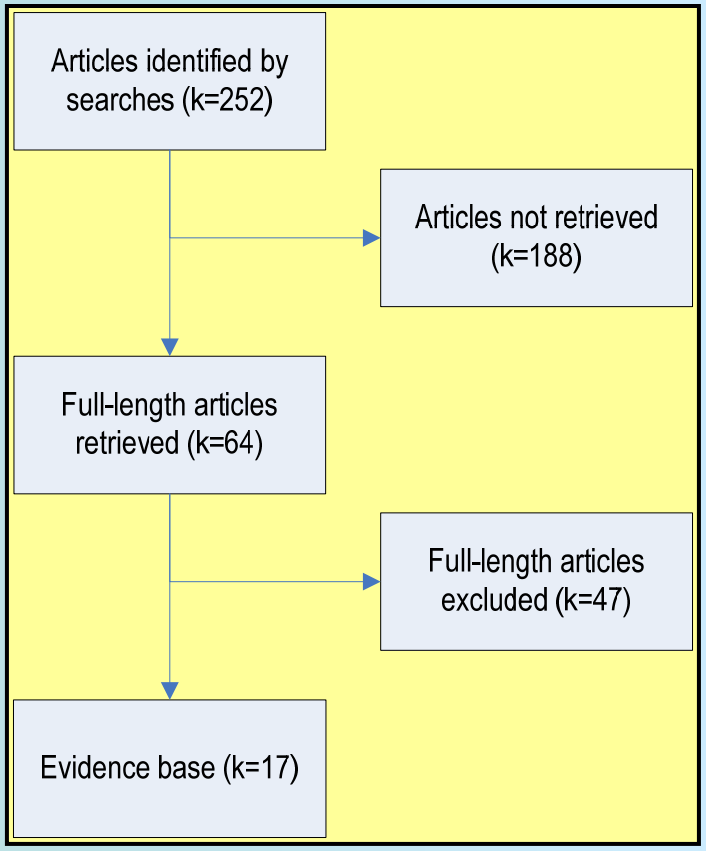
Searches

Name of database	Date limits	Platform/provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	2003 through April 30, 2007	OVID
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	2003 through 2007 Issue 2	www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	2003 through 2007 Issue 2	www.thecochranelibrary.com
The Cochrane Central Register of Controlled Trials (CENTRAL)	2003 through 2007 Issue 2	www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	2003 through 2007 Issue 2	www.thecochranelibrary.com
ECRI Institute Library Catalog	2003 through 2007	ECRI Institute
Embase (Excerpta Medica)	2003 through April 30, 2007	OVID

Searches

Name of database	Date limits	Platform/provider
Health Technology Assessment Database (HTA)	2003 through 2007 Issue 2	www.thecochranelibrary.com
Medline	2003 through April 30, 2007	OVID
National Guideline Clearinghouse (NGC)	2003 through April 30, 2007	www.ngc.gov
NHS Economic Evaluation Database (NHS EED)	2003 through 2007 Issue 2	www.thecochranelibrary.com
PsycINFO	2003 through April 30, 2007	OVID
PubMed (Pre Medline)	Premedline[sb} Searched March 30, 2007	www.pubmed.gov

Key Question 1: Crash Risk



- 17 studies included
- 2 studies - CMV drivers
- All case-control
- Quality = Low/moderate

Key Question 1: Crash Risk Among CMV Drivers

- Howard et al. 2004 (Quality = Low)
  - Australia
  - 2,342 of 3,268 (72%) responded
  - CMV drivers with sleep apnea syndrome (symptom diagnosis [Multivariable Apnea Prediction Score (MAPS)] ≥ 5 + ESS ≥ 11) vs. CMV drivers not diagnosed with sleep apnea syndrome (controls)
  - Drivers diagnosed with sleep apnea syndrome (MAPS ≥ 0.5 and ESS Score ≥ 11) found to be at an increased risk for crash (OR = 1.3, 95% CI: 1.00-1.69)

Key Question 1: Crash Risk Among CMV Drivers

- Stoohs *et al*. 1994 (Quality = Moderate)
  - A cross-sectional population of 90 CMV drivers 20-64 years of age who agreed to undergo overnight recordings (Mesam IV)
  - Recordings consisted of:
    - Oxygen saturation
    - Heart rate
    - Snoring sounds
    - Body position/movement
  - Crash data – self reported via questionnaire
  - Main outcome measures included:
    - Crash rate over previous 5 years
    - Oxygen Desaturation Index (ODI)
    - Total sleep time

Key Question 1: Crash Risk Among CMV Drivers

Explanatory Variable	Findings	Significant (P <0.05)?
Crashes and sleep-disordered breathing (SDB)	Drivers diagnosed with SDB (ODI $\geq$ 10) accounted for 23 of the 42 crashes, whereas drivers without SDB (ODI < 10) caused 19 of all reported crashes.	No
	Drivers with SDB caused twice as many crashes/mile driven (0.085 crashes/10,000 miles) than drivers without SDB (0.046 crashes/10,000 miles).	No
Crashes and severity of SDB	Though crash frequency was about 100% higher in drivers with SDB: increasing severity of SDB was not significantly associated with an increase in crash frequency.	No
Crashes and excessive daytime sleepiness (EDS)	There was significantly higher crash frequency in drivers complaining of EDS (0.18 crashes/10,000 miles) as opposed to drivers without a complaint of EDS (0.06 crashes/10,000 miles).	Yes
	Using the scores for self-reported sleepiness, the isolated use of EDS as a predictive parameter for the occurrence of crashes had a sensitivity of 9% and a specificity of 92%.	NA
Crashes and obesity	Non-obese drivers (BMI < 30 kg/m^2) had a mean of 0.045 crashes/10,000 miles compared to a mean of 0.1 crashes/10,000 miles in obese truck drivers.	Yes
	Non-obese truck drivers without SDB caused 77% more crashes/10,000 miles than non-obese drivers with nocturnal breathing abnormalities.	No
	Obese truck drivers with SDB caused 45% more crashes/mile driven than obese drivers without SDB.	No
	Using the scores for obesity ($\geq$ 30 kg/m^2) as a predictor for driving crashes, this predictor had a sensitivity of 49% and a specificity of 71%.	NA

Key Question 1: Crash Risk Among CMV Drivers

Explanatory Variable	Findings	Significant (P <0.05)?
Crashes, EDS, and obesity	When combined, EDS and a BMI $\geq$ 30 kg/m^2 had a sensitivity of 53% and a specificity of 68% in predicting drivers with crashes.	NA
Crashes, SDB, EDS, and obesity	When combined, SDB, EDS and a BMI $\geq$ 30 kg/m^2 had a sensitivity of 76% and a specificity of 35% in predicting drivers with crashes.	NA

Key Question 1: Crash Risk

- **CMV drivers with OSA are at an increased risk for a crash when compared to their counterparts who do not have the disorder (SoE: Minimally Acceptable)**
  - **A precise estimate of magnitude of this increased risk cannot be determined at this time**

Key Question 1: Crash Risk: Findings of Rate Ratio (RR) Studies

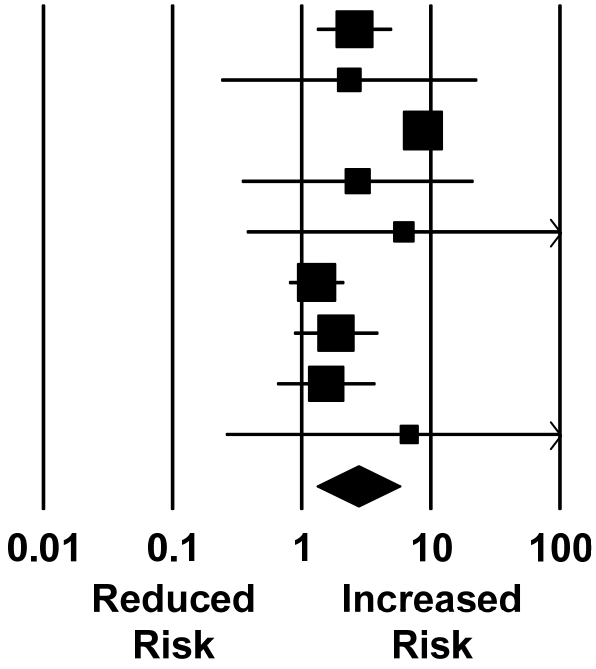
- 15 studies of general motor vehicle drivers
- RR studies = crash rate among individuals with OSA vs. crash rate among comparable individuals without OSA
- Overall quality = Low
- We wished to pool data from studies
- 6 studies not pooled because not enough data was presented to determine the crash rate ratio and 95% confidence intervals
- Crash data from 9 studies pooled

Key Question 1: Crash Risk (Random-Effects Meta-Analysis)

Study name	Rate ratio	Lower limit	Upper limit	Z-Value	p-Value
Barbe	2.570	1.304	5.065	2.727	0.006
Shiomi	2.342	0.237	23.159	0.728	0.467
Horstmann	8.719	6.179	12.303	12.326	0.000
Lloberes	2.720	0.342	21.658	0.945	0.345
Findley 2000	6.195	0.373	102.902	1.272	0.203
George	1.306	0.791	2.158	1.043	0.297
Stoohs	1.848	0.865	3.947	1.586	0.113
Haraldsson	1.551	0.641	3.756	0.973	0.330
Findley 1988	6.833	0.257	181.694	1.148	0.251
	2.722	**1.295**	**5.722**	**2.642**	**0.008**

Statistics for each study

Rate ratio and 95% CI



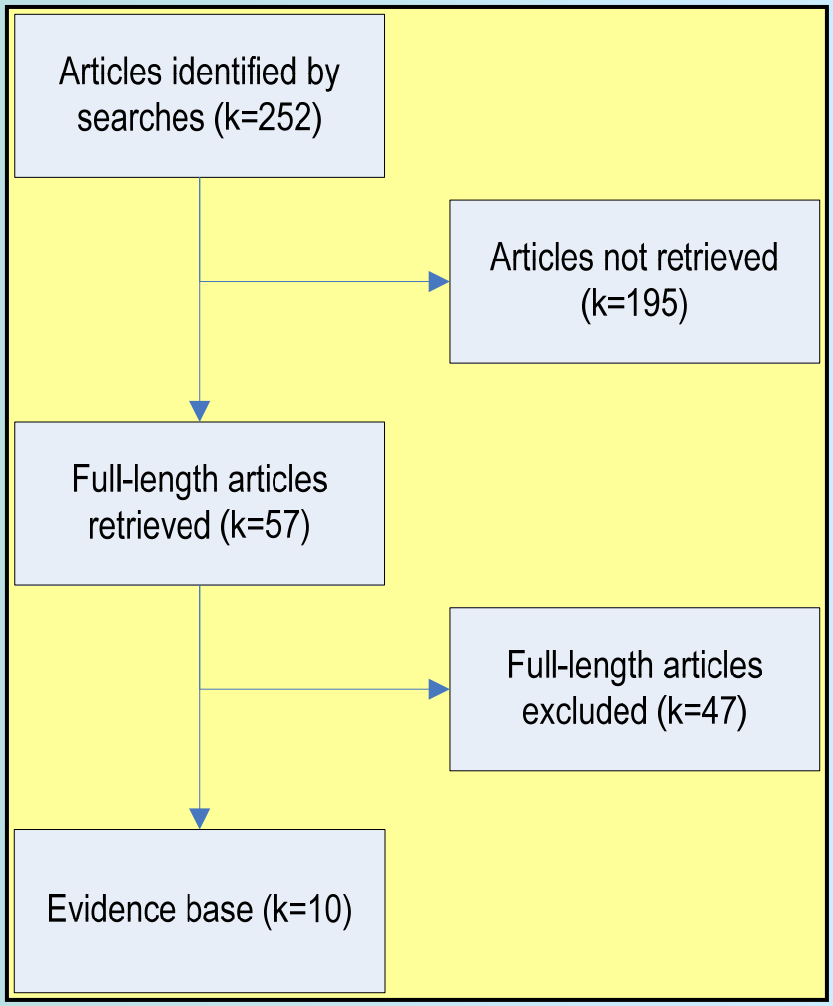
Key Question 1: Crash Risk: Findings of Rate Ratio (RR) Studies

- Findings of remaining 6 studies not included in MA do not contradict findings of MA
- Sensitivity analyses did not overturn findings of MA
- No evidence of publication bias found
- Findings robust

Key Question 1: Crash Risk

- As a group, drivers with obstructive sleep apnea are at an increased risk for a motor vehicle crash when compared with comparable drivers who do not have the disorder (SoE: Strong)
  - Precise estimate of magnitude of this increased risk not calculated
  - Crash Risk Rate in region of 1.30 to 5.72

Key Question 2: Risk Factors and Crash Risk



- 10 studies included
- All case-control studies
- One specific to CMV drivers
- Overall quality = Low

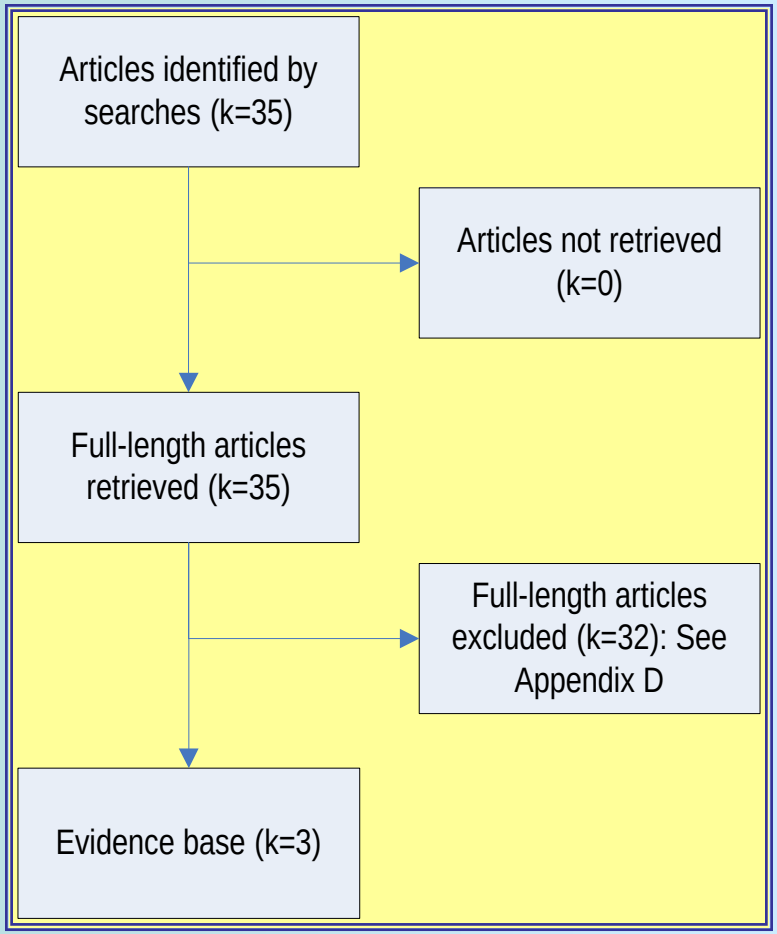
Key Question 2: Risk Factors and Crash Risk

Study	Year	Potential Risk Factors Examined				
		Daytime Sleepiness	Severity of disordered respiration	Oxygen Saturation	Body Mass Index	Cognitive/ Psychomotor Function
Commercial Motor Vehicle Drivers						
Stoohs et al.	1994	√	√		√	
Non-Commercial Motor Vehicle Drivers						
Shiomi et al.	2002		√			
Turkington et al.	2001	√	√			√
Horstmann et al.	2000	√	√		√	
Yamamoto et al.	2000	√	√	√	√	
George and Smiley	1999		√			
Barbe et al.	1998	√	√	√		√
Noda et al.	1998	√	√	√		
Engleman et al.	1996		√	√		
Aldrich	1989	√	√	√		
Number of studies (k=)		6	10	5	3	2

Key Question 2: Risk Factors and Crash Risk

- **Because of a lack of reproducibility studies, we refrain from drawing an evidence-based conclusion about OSA-related risk factors for crash in a CMV driver population**
- **Four factors have consistently been shown to be associated with crash risk among the general driver population:**
  - **Severity of disordered respiration during sleep (as measured by the AHI or the RDI)**
  - **Presence and degree of daytime sleepiness (as measured using ESS but not MSLT or MWT)**
  - **Blood oxygen saturation levels**
  - **Body mass index (BMI)**

Key Question 3: Awareness of Identified Risk Factors



- 3 studies
- All case-series
- Different approaches to same problem

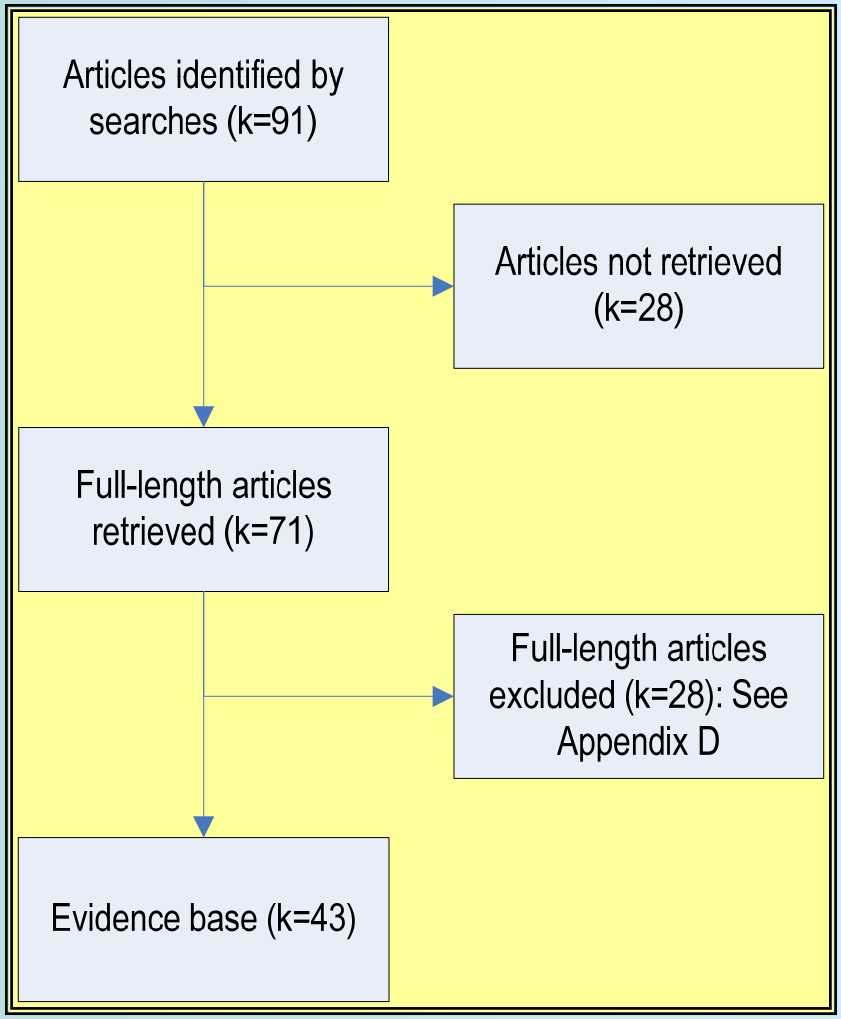
Key Question 3: Awareness of Identified Risk Factors

- One study found that when individuals with moderate-to-severe OSA re-evaluated the degree of sleepiness they had experienced prior to the onset of treatment (measured via the Epworth Sleepiness Scale), the pre-treatment level of sleepiness was reassessed as being much higher than originally reported
- One study found no correlation between Epworth Sleepiness Scale and Mean Sleep Latency Test scores, suggesting a disconnect between subjective and objective measures of sleepiness
- One study found no difference in Epworth Sleepiness Scale scores of individuals with OSA and ESS scores estimated by their partners

Key Question 3: Awareness of Identified Risk Factors

- **Individuals with OSA may not be aware of the extent to which they are affected by daytime sleepiness (SoE: Minimally Acceptable)**

Key Question 4: Diagnosis and Severity Stratification



- 43 studies
  - 42 studies assessed the diagnostic performance of a portable sleep monitoring system
  - 1 study assessed the effectiveness of a clinical model in addition to a portable sleep monitoring system
    - This was the only study to have enrolled only CMV drivers
- Moderate-to-high quality

Key Question 4: Diagnosis and Severity Stratification

Portable Device Level	Severity	K=	Diagnostic OR (D)	Slope	Homogeneous?	Summary Sensitivity at mean threshold	Summary Specificity at mean threshold	Summary ROC
II	AHI≥10	1	NC	NC	NA	80.0	90.0	NA
	AHI≥20	1	NC	NC	NA	100.0	100.0	NA
III	AHI≥5	8	6.8469	0.047	No	98.8 (95.5-99.7)	92.8 (77.4-98.0)	Figure 18
	AHI≥10	12	4.2516	-0.34692	No	89.0 (84.0-92.6)	89.9 (85.2-93.3)	Figure 19
	AHI≥15	11	4.2428	-0.3869	No	90.2 (84.8-93.8)	87.0 (80.3-91.7)	Figure 20
	AHI≥20	12	4.0601	-0.0394	No	89.5 (86.4-91.9)	87.1 (83.5-90.0)	Figure 21
	AHI≥25	1	NC	NC	No	44.0	81.0	NA
	AHI≥30	3	3.1918	-1.0407	No	83.2 (69.4-91.6)	87.0 (75.3-93.6)	Figure 22
	AHI≥35	0	NA	NA	NA	NA	NA	NA
	AHI≥40	4	5.6825	0.7383	No	82.7 (58.9-94.1)	95.4 (86.2-98.6)	Figure 23
IV	AHI≥5	7	4.0245	-0.2613	No	90.0 (86.8-92.5)	84.4 (79.7-88.1)	Figure 24
	AHI≥10	17	4.3044	-0.2540	No	92.1 (89.5-94.1)	83.7 (78.9-87.6)	Figure 25
	AHI≥15	15	4.2310	0.1045	No	84.5 (79.4-88.6)	92.1 (89.1-94.3)	Figure 26
	AHI≥20	7	4.4236	0.3255	No	87.6 (82.0-91.6)	91.2 (87.6-94.2)	Figure 27
	AHI≥25	0	NA	NA	NA	NA	NA	NA
	AHI≥30	5	3.9701	0.1574	No	64.6 (54.9-73.2)	95.2 (93.0-96.8)	Figure 28
	AHI≥35	0	NA	NA	NA	NA	NA	NA
	AHI≥40	0	NA	NA	NA	NA	NA	NA

Key Question 4: Diagnosis and Severity Stratification

- **No model or psychometric instrument has been shown to accurately stratify individuals with OSA by disease severity (a surrogate marker for crash risk)**
- **A number of portable sleep monitoring systems, though not as accurate as the current reference standard (PSG), offer an alternative method for assessing the severity of OSA in a large number of individuals at a relatively low cost**
  - It is not clear whether these systems are accurate enough to be considered acceptable alternatives to PSG for stratifying individuals by OSA severity for the purposes of making decisions about the fitness of an individual to drive a CMV
  - A formal decision and cost-effectiveness analyses should be performed to fully address this issue

Key Question 5: Treatment Effectiveness

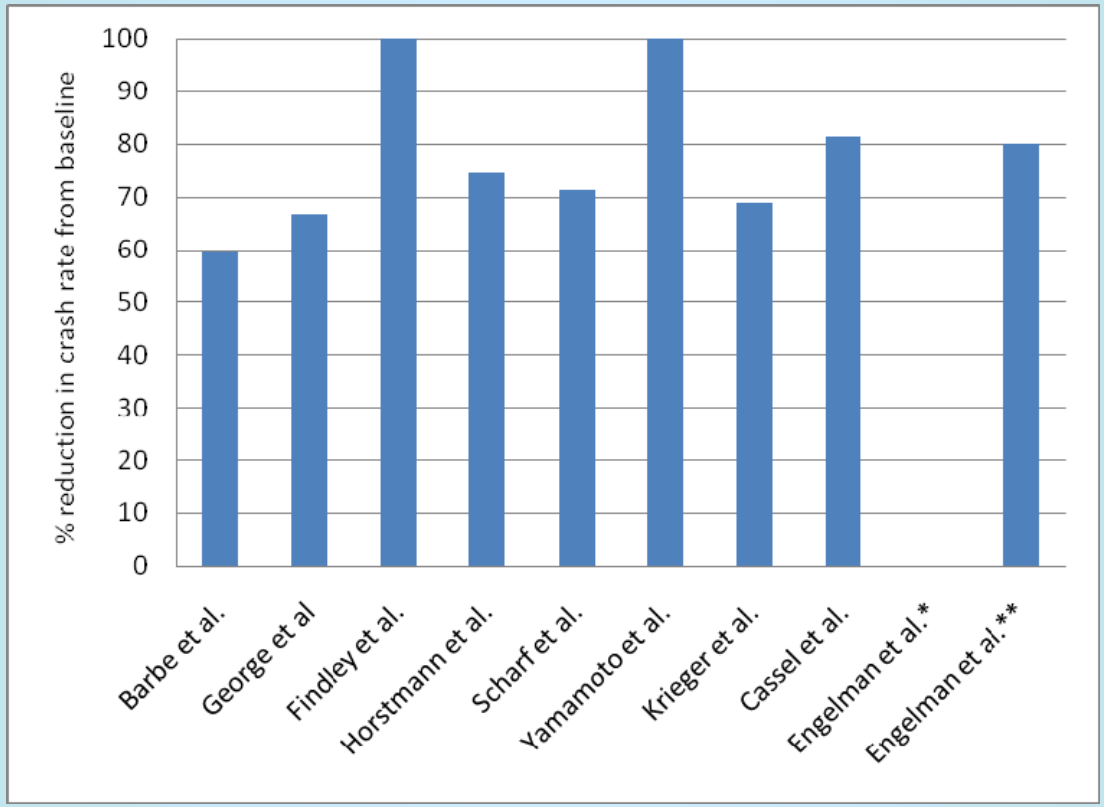
- 3 separate evidence bases developed
  - Crash – 9 studies
    - All CPAP
  - Simulated driving performance – 10 studies
    - 8 CPAP
    - 1 medication (theophylline)
    - 1 dental appliance (mandibular advancement)
    - 1 surgery (UPPP)
  - Indirect measures – 48 studies
    - 3 Behavioral modification
    - 32 CPAP
    - 2 Dental appliances
    - 8 medication
    - 6 surgery

Key Question 5: Treatment Effectiveness

	Behavioral modification (weight loss)	CPAP	Dental Appliances	Medications				Surgery		
			Mandibular advancement splints	Theophylline	Modafinil (or armodafinil) as adjunct to CPAP	Mirtazepine	Salmeterol	UPPP	LAUP	TCRFTA
Crash	No evidence	***	No evidence	No evidence	No evidence	No evidence	No evidence	No evidence	No evidence	No evidence
Simulated Driving	No evidence	**	*	*	No evidence	No evidence	No evidence	*	No evidence	No evidence
AHI	*	***	*	?	No evidence	*	?	No evidence	?	?
Cognitive/ Psychomotor Function	No evidence	?	?	No evidence	No evidence	No evidence	No evidence	?	?	No evidence
Daytime sleepiness (ESS)	No evidence	***	?	No evidence	?	No evidence	No evidence	*	?	?
Daytime sleepiness (MSLT)	No evidence	?	No evidence	No evidence	?	No evidence	No evidence	No evidence	No evidence	No evidence
Daytime sleepiness (MWT)	No evidence	No evidence	?	No evidence	*	No evidence	No evidence	No evidence	No evidence	No evidence
Oxygen Saturation	?	***	*	?	No evidence	?	?	?	No evidence	?
24-hour systolic BP	No evidence	**	No evidence	No evidence	No evidence	No evidence	No evidence	?	No evidence	No evidence
24-hour diastolic BP	No evidence	**	No evidence	No evidence	No evidence	No evidence	No evidence	?	No evidence	No evidence

Key Question 5: Treatment Effectiveness

% Reduction in Crash Rate Following CPAP



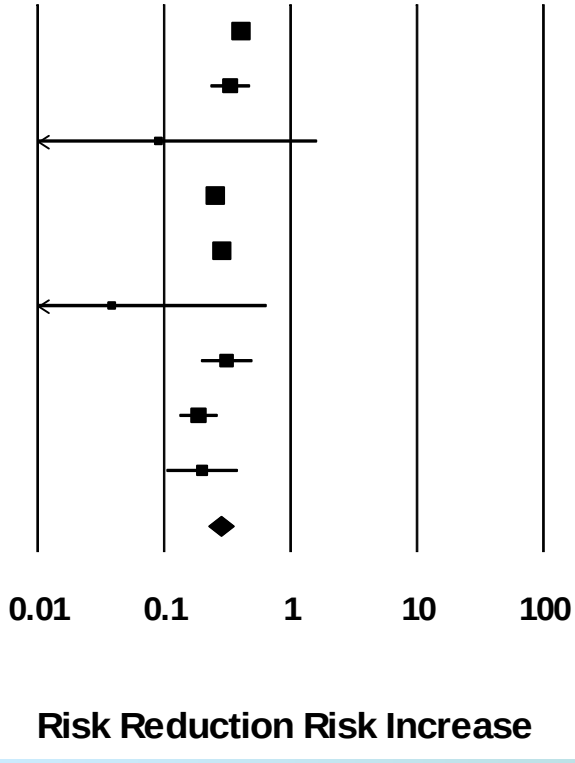
*Any non-injurious crash

**Any injurious crash

Key Question 5: Treatment Effectiveness

- Crash risk reduced by approx 72% following CPAP

Study name	Rate ratio	Lower limit	Upper limit	Z-Value	p-Value
Barbe	0.407	0.370	0.447	-18.566	0.000
George	0.333	0.231	0.482	-5.850	0.000
Findley	0.090	0.005	1.631	-1.629	0.103
Horstmann	0.255	0.232	0.279	-29.279	0.000
Scharf	0.286	0.250	0.327	-18.292	0.000
Yamamoto	0.039	0.002	0.649	-2.260	0.024
Krieger	0.313	0.194	0.503	-4.797	0.000
Cassel	0.188	0.131	0.267	-9.246	0.000
Engleman (injury)	0.200	0.104	0.385	-4.811	0.000
	0.278	0.223	0.348	-11.214	0.000



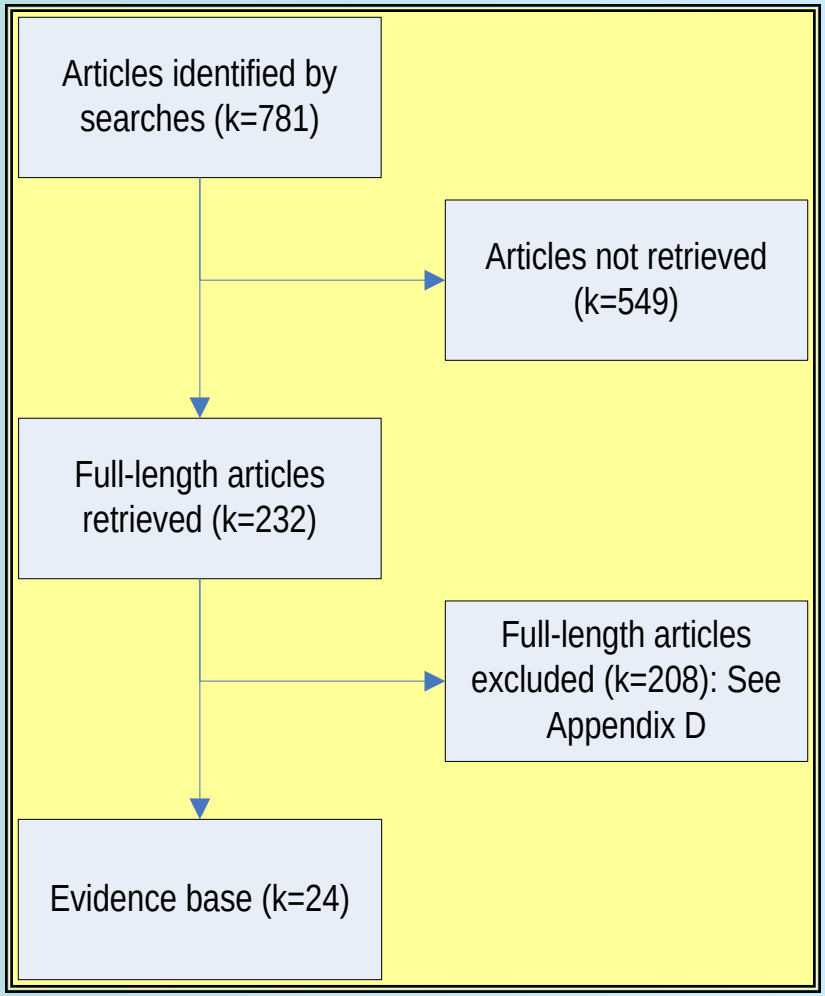
Key Question 5: Treatment Effectiveness

- But is this reduction large enough to reduce crash risk to "normal" levels?

Reference	Year	Crash rate after treatment	Time period	Non-OSA control crash rate	Time period	Crash Rate Ratio (95% CI)	P-value
Barbe et al.(68)	2006	3.74 per 1,000,000 km	2 years	1.74 per 1,000,000 km	2 years	2.15 (1.87 to 2.48)	<0.001
George et al.(151)	2001	0.06 crashes per person/year	3 years	0.07 crashes per person/year	3 years	0.86 (0.56 to 1.32)	0.487
Findley et al.(72)	2000	0.00 crashes per person/year	2 years	0.01 crashes per person/year	2 years	0.41 (0.02 to 11.01)	0.595

- The results are not clear!
- Indirect measures suggest that not all individuals will attain normal levels of function

Key Question 6: Time to Reach Optimal Effectiveness

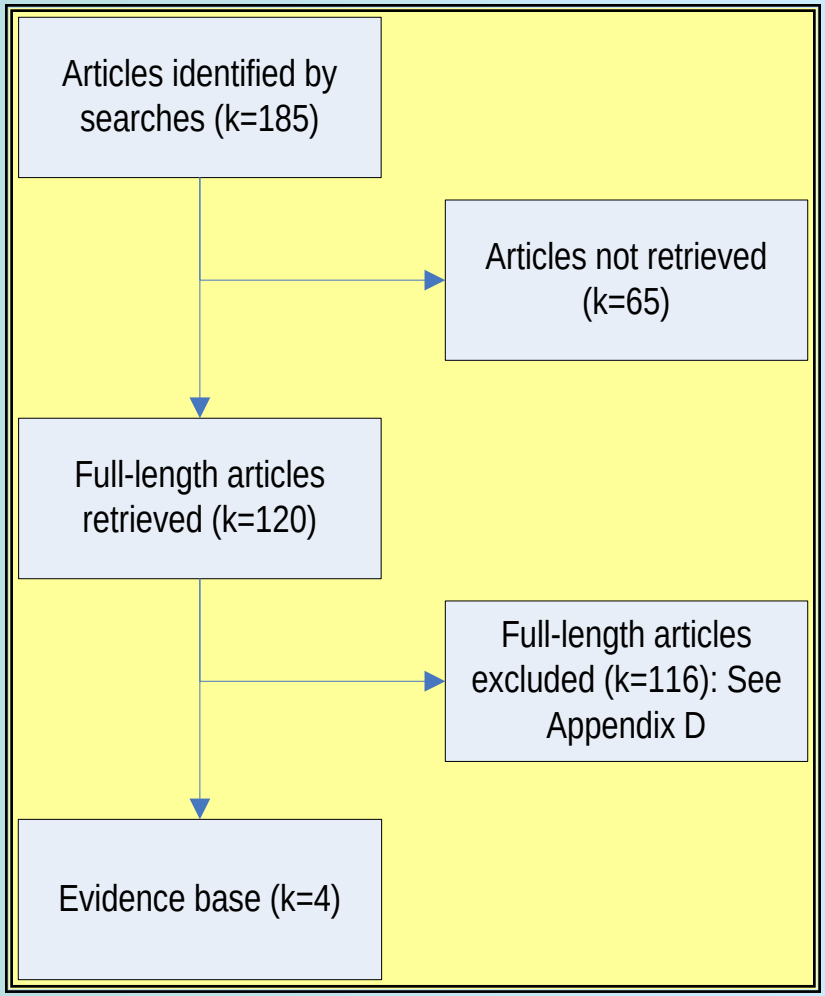


- 24 studies
  - 12 CPAP
  - 1 CPAP & Oral Appliances
  - 1 CPAP and Medication
  - 9 Medication
  - 1 Oral Appliances
- High quality: 8
- Moderate quality: 14
- Low quality: 2

Key Question 6: Time to Reach Optimal Effectiveness

- **The impact that CPAP has on crash risk reduction among individuals with OSA is seen after as little as one night of treatment (SoE: Minimally Acceptable)**
  - **Simulated driving performance, severity of disordered respiration, blood oxygen saturation, and some (but not all) measures of cognitive and psychomotor performance improve significantly following a single night of treatment**
  - **Exactly how many nights of treatment are required until CPAP exerts maximum benefit is not known but evidence suggests <2 weeks**

Key Question 7: Time to Deteriorate



- 4 studies
- All 4 assessed effects of withdrawal from CPAP

Key Question 7: Time to Deteriorate

- **Cessation of CPAP leads to a decrease in simulated driving ability and increases in both OSA severity and daytime sleepiness (SoE: Minimally Acceptable)**
  - **The exact rate at which deterioration occurs cannot be determined; however, this deterioration may occur as soon as 24 hours following cessation of treatment**