The effect of intensive care unit out-of-hours admission on mortality

A systematic review and meta-analysis

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Running title: Out of hours admissions to the ICU

Word count:

Key words: Organization, healthcare services research, outcomes

Funding: None.

Conflict of interest: None

Abstract

Objective

Organizational factors are associated with outcome of critically ill patients and may vary by time of day and day of week. We aimed to identify the association between out-of-hours admission to critical care and mortality.

Data Sources

MEDLINE (via Ovid), and EMBASE (via Ovid)

Study Selection

We performed a systematic search of the literature for studies on out-of-hours adult general intensive care unit (ICU) admission on patient mortality.

Data Extraction

Meta-analyses were performed and Forest plots drawn using RevMan software. Data are presented as odd ratios (OR (95% confidence intervals), p-values).

Data synthesis

A total of 16 studies with 902551 patients were included in the analysis with a crude mortality of 18.2%. Fourteen studies with 717,331 patients reported mortality rates by time of admission and 11 studies with 835,032 patients by day of admission. Admission to ICU at night was not associated with an increased odds of mortality compared to admissions during the day (OR 1.04(0.98-1.11); p=0.18). However, admissions during the weekend were associated with an increased odds of death compared to ICU admissions during weekdays (1.05(1.01-1.09), p=0.006). Increased mortality associated with weekend ICU admissions compared to weekday ICU admissions were limited to North American countries (1.08(1.03-1.12); p=0.0004). The absence of a routine overnight on site intensivist was associated with increased mortality among weekend ICU admissions compared to weekday ICU admissions (1.11(1.00-1.22); p=0.04) and nighttime admissions compared to daytime ICU admissions (1.11(1.00-1.23); p=0.05).

Conclusion

Adjusted risk of death for ICU admission was greater over the weekends compared to weekdays. The absence of a dedicated intensivist on site overnight may be associated with increased mortality for acute admissions. These results need to be interpreted in context of

the organization of local healthcare resources before changes to healthcare policy are implemented.

Introduction

A number of organizational factors are associated with outcome of critically ill patients. This includes improved outcomes with ‘closed’ models of critical care (1), presence of dedicated intensivists (2-4), intensivist staffing patterns (5, 6), and adequate nursing numbers (7). Initial resuscitation efforts of critically ill patients have a significant impact on patient outcome and should. As critically ill patients present at any time of day, provision of intensive care unit (ICU) resources should reflect this. The association between out-of-hours (evening, nighttime, weekday and weekend) admissions to ICUs has been investigated. Previous meta-analysis in 2010 has demonstrated that nighttime admission was not associated with an increase in mortality, while patients admitted at the weekend had a significantly increased odds of mortality (8). However, these results were attributable primarily one study that did not include analysis by time of day (9). With the growing interest and emphasis on healthcare services research, there have been several additional studies with large patient numbers investigating the effect of out of hours ICU admission and patient mortality. Any differences in mortality by time of day or day of week is likely to have significant influence on healthcare policy, medical insurance, and workforce planning.

We performed an up to date systematic review and meta-analysis to investigate the association between out-of-hours admissions to critical care and patient mortality. Secondary analyses included the effect of country/ region of study and the presence of an on site intensivist.

Methods

Eligibility criteria

All studies investigating the association of time of day and/or day of week on ICU admission were included. Only studies reporting mortality as the primary outcome were included. Studies amalgamating evenings/nights and weekends as 'out-of-hours', without analyzing them separately, were excluded. Only studies involving adult general intensive care populations were included, and cardiac, trauma and pediatric intensive care were excluded.

Information sources

A systematic literature search of MEDLINE (via Ovid), and EMBASE (via Ovid) was conducted to identify suitable studies. Only articles in the English language were considered. Date restrictions were not applied to the MEDLINE searches or EMBASE. The last search update was in September 2016.

Search strategy

We included the following search term; (mortality OR death OR die OR died OR readmission) AND (ITU OR ICU OR AICU OR intensive care OR critical care OR intensive therapy unit) AND (post OR after OR following OR discharge OR admission OR ward OR in hospital OR transfer from) AND (out-of-hours OR off-hour OR night time OR evening). In addition to searching electronic databases, previous review articles on the subject were hand-searched for further references.

Methodological quality of included studies

Methodological quality of included studies was assessed using criteria described by the "STrengthening the Reporting of OBservational studies in Epidemiology" (STROBE) criteria for cohort studies (http://www.strobe-statement.org/index.php?id=strobe-home). Studies were not excluded based on STROBE scores.

Data extraction

Two investigators independently screened both the titles and abstracts to exclude non-pertinent studies. Relevant full text articles were then retrieved and analyzed for eligibility against the pre-defined inclusion criteria. Information from selected studies was extracted using a standardized data collection form. Data was collected independently by two different investigators (MG and SG) and discrepancies resolved by a third author (NA). Hospital or ICU mortality was reported in all the included articles and was the primary outcome of our study. Where both hospital and ICU mortality is reported, we choose hospital mortality as an outcome.

Calculation of adjusted odds ratios

Adjusted odds ratios were not stated in all studies. Where standardized mortality ratio (SMR) was quoted, observed mortality and SMR were used to calculate risk-adjusted mortality from which the adjusted OR was calculated. Where absolute risk difference in mortality was quoted, adjusted odds ratio was calculated. In studies dividing the day into morning, evenings, and night time, we combined morning and evening data into daytime data. An overall estimate was calculated from the available ORs for weekend night and weekday night using a fixed-effects model and the inverse-variance method.

Statistical analysis

We combined individual study data (adjusted OR and 95% CI) and mortality was analyzed using the DerSimonian and Laird random effects model. Results are presented as an odds ratio (OR) with 95% confidence intervals (CI). A random effects model was used to analyse the data. The reference period of the OR was taken as the period 'in-hours' (day time or weekday as appropriate). The meta-analysis was carried out using review manager ('Revman') for Mac (version 5.1, Cochrane collaboration, Oxford, UK). Statistical heterogeneity was assessed using the I^2 methodology. When an I^2 value of >50% was present, heterogeneity and inconsistency was considered significant and >75% very high (10). All p-values were two-tailed and considered statistically significant if <0.05.

Results

Included trials

The search strategy used in this study produced 475 potential titles (Supplemental Figure 1). After screening of titles and abstracts, 40 references were identified as relevant to the association between ICU admission time of day/day of week and mortality. After further screening of titles and abstracts against our inclusion criteria, 29 references were retrieved for full text analysis. Detailed full text evaluation excluded 9 studies, as they were pediatric studies (11-16), readmissions(17), not in English (18), or a correspondence (19). Three studies did not report separate outcomes by time of day or day of week (20-22). An additional 6 studies were identified by hand searching (9, 23-27).

A total of 16 studies reported outcomes by day of admission and/or time of admission and were included (9, 23-37) (Supplemental Table 1). Nine studies reported mortality by day of admission and time of admission, whilst 5 studies reported outcomes by time of admission only and 2 studies reported outcomes by day of admission only (Supplemental Table 1). There were a total of 902,551 patients in the 16 studies with a crude mortality of 18.2% (9, 23-37). Study size varied from 195 to 245,057 patients, and data collection dates spanned from 1994 to 2015. Four studies provided data only on ICU mortality (23, 25, 35, 37) and the other studies reported hospital mortality. Mortality rate varied from 4% to 44% (23, 25). There was heterogeneity in the inclusion criteria, and definition of 'night hours' between individual studies.

Time of day and day of week

Fourteen studies investigated the association between time of day of ICU admissions and mortality (22, 23, 25-37) (Table 2). The 14 studies exploring admissions by time of day had a total of 717,331 patients with a crude mortality of 144432 (20.3%). 390,722 (54.5%) patients were admitted during daytime hours and 326,609 (45.5%) patients were admitted during nighttime hours. Crude mortality was 75,678 (19.4%) for daytime admissions and 69,754 (21.4%) nighttime admissions (Table 1). Adjusted for baseline variables, there was no increase in mortality associated with admission to ICU at night (1.04 (0.98-1.11); p=0.18) (Figure 1a). There was significant heterogeneity between studies (I^2 = 93%, p<0.001).

Twelve studies including 837,460 patients investigated the association between day of week of ICU admissions and mortality (9, 24, 26-31, 33, 35-37) (Table 2). The crude mortality was 145,536 (17.4%). Patients admitted to ICU on a weekday had a mortality rate of 105,961 (16.4%) compared to patients who were admitted at the weekend who had a mortality rate of 39,575 (20.9%). Adjusted weekend admissions were associated with a higher mortality compared to weekday admissions (1.05 (1.01-1.09), p=0.006) (Figure 1b). There was significant heterogeneity between studies (I^2 = 76%, p<0.001).

Country of study

Seven studies were based in European countries (26, 28, 30, 32, 35-37), four North American (9, 24, 31, 33), one Australian (29), and three Asian countries (25, 27, 34), and one North African country (23). All seven European studies, two North American studies, the three Asian studies, and the Australian and North African studies reported mortality by time of day. The seven studies from European countries (26, 28, 30, 32, 35-37) (1.02 (0.98-1.06); p=0.38), two North American studies (31, 33) (0.93 (0.44-1.99); p=0.86), and three Asian studies (25, 27, 34) (1.31(0.81-2.11); p=0.28) did not demonstrate any increase in mortality risk associated with nighttime admissions compared to daytime admissions (Figure 2a).

Five of the eight European studies (26, 28, 30, 35, 36), three of the four American studies (9, 24, 31), the one Australian study (29), and two of the three Asian studies (27, 34) reported mortality risk by day of week. The five studies from Europe (1.05 (0.99-1.13); p=0.13), and two Asian countries (0.89(0.63-1.25); p=0.49) did not demonstrate any increased odds of death among weekend admissions compared to weekday admissions. The three North American studies demonstrated an increased odds of death among weekend admissions compared to weekday admissions (1.08(1.03-1.12); p=0.004) (Figure 2b). There was significant homogeneity among North American studies (I^2 = 0%, p=0.75), and Asian studies (I^2 = 0%, p=0.45) but not among European studies (I^2 = 88%, p<0.001) reporting ICU admission and mortality by day of week.

Routine overnight onsite intensivist cover

There are differences in the organizational structures of the ICUs. There was significant heterogeneity in the patterns of staffing overnight (Supplementary Table 1). We defined 'overnight on site intesivits presence' as the presence of a trainee or fellow in critical care who was routinely based on the intensive care unit overnight. Where overnight on site cover was provided by fellows without critical care training, or where fellows were expected to routinely cover services outside the ICU, we did not consider this as 'overnight on site intesivits presence'. The presence of on site intensive care cover during weekend days was almost universal.

Only 7 studies reported the presence of an intensivist overnight (22, 24, 27, 30, 31, 33, 37), 6 studies did not have any consistent intensivist cover overnight (23, 25, 26, 29, 32, 34, 35), and 4 studies did not report intensivist staffing overnight (9, 28, 29, 36).

The routine presence of onsite intensivist cover overnight was associated with a similar odds of mortality for daytime and nighttime admissions (0.94(0.68-1.30); p=0.72), although there was significant heterogeneity between studies (I^2=95%; p<0.001) (Figure 3a). The absence of intensivist cover overnight was associated with an increased odds of death among nighttime admissions compared to daytime admissions (1.11(1.00-1.23); p=0.05), with only moderate heterogeneity between studies (I^2=53%; p=0.06).

The routine presence of an onsite intensivist cover overnight was associated with a similar odds of mortality for weekend and weekday admissions (1.05(0.98-1.13); p=0.16) with no heterogeneity between studies (I^2=0%, p=1.00) (Figure 3b). However, the lack of an onsite intensivist cover overnight was associated with a increased odds of mortality for weekend and weekday admissions (1.11 91.00-1.22); p=0.04) with minimal heterogeneity between studies (I^2=32%; p=0.23).

Quality of studies

A total of 32 points on the STROBE checklist were assessed. We excluded the STROBE recommendations 6b ("For matched studies, give matching criteria and number of exposed and unexposed") and 16c ("If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period") from the score as these were not relevant. The median STROBE score for the 17 studies was 28 with a minimum score of 24 and a maximum score of 32.

Discussion

The adjusted odds of death is greater among patients admitted to the ICU during the weekends compared to weekdays. In contrast, there was no influence of ICU admission time of day on mortality. The pooled data of this meta analysis corrects for any differences in illness severity and case mix between patients admitted by time of day or day of week.

We performed two independent subgroup analysis to investigate the effect of country of study and the effect of a routine onsite intensivist cover overnight. Admission to ICU during the daytime or nighttime was not influenced by the country of study. However, admission to ICU during the weekend compare to the weekdays was associated with increased mortality in North American countries and the single Australian study. The lack of heterogeneity among North American studies reporting mortality by day of admission suggests that this finding is significant. Admission to ICU during the weekends compared to weekdays was associated with increased mortality where there was no routine intensivist cover overnight, with a similar trend among overnight admissions compared to daytime admissions.

The observation of increased odds of mortality associated with weekend ICU admission in North American countries but not European countries are likely to be explained by multiple differences between American and European intensive care services. This includes the availability of ICU beds (38), threshold for ICU admission (39, 40) , and utility of ICU beds for terminal hospitalizations (41). Differences in working patterns may also be a factor. Historical data has shown that the presence of night-time ICU doctors varies- from 40% of ICUs in Netherlands, Norway and Finland to 90-100% in France, Italy, Portugal or Spain (42). ICU cover at night time in the UK is variable (43). In contrast, where majority of American ICUs have low intensity staffing, only 9% of ICUs have a night-time ICU doctor (44).

Overall, we did not find an increased risk of mortality associated with overnight ICU admissions compared to daytime admissions. However, in studies that lacked overnight intensivist cover, there was an associated increase in odds of mortality among overnight ICU admissions which approached statistical significance. Observational single centre studies investigating staffing patterns on ICU have not demonstrated any consistent association between the presence of a night-time ICU doctor and patient survival (45-47), and a randomized control trial of nighttime intensivist staffing was not associated with either ICU/hospital mortality or length of stay (48). Two large databases across 49 American ICUs demonstrate that night-time ICU doctor staffing in addition to a high intensity daytime staffing did not reduce ICU mortality (49). The reduction in mortality may be dependent on the intensity staffing throughout the day rather than the presence of intensivist overnight. Within a high-intensity model, 24-hour in-hospital intensivist coverage was not associated with a reduction in mortality (50).

The lack of an onsite intensivist overnight was associated with increased odds of death among weekend ICU admissions compared to weekday ICU admissions. Due to heterogeneity and limitations in data reporting between studies, it was not possible to assess the interaction between day of week and time of day, or to assess the interaction between ICU staffing patterns and day of week/ time of day mortality differences for ICU admissions.

A premise to this study was based on the effect of the unpredictability of emergency admissions during periods of reduced staffing either within the ICU or the hospital. However, only two studies excluded non-emergency cases in their analysis (28, 35). Neither of these studies demonstrated an adjusted mortality risk associated either with admissions by time of day or day of week. It is not possible to ascertain the effect of elective admissions from other studies due to lack of reporting.

Critically ill patients require timely diagnostic and therapeutic interventions, particularly following admission when they are likely to be unstable and require immediate work-up. Delayed intensive care admission (often defined as greater than four hours from decision to admit until time of admission) is associated with increased odds of mortality (51-54). Delayed admission may in fact occur more frequently during weekdays compared to weekends, though is likely to vary in different healthcare systems (28). Whilst some critical care units may have fewer staff out of hours, there is still an adequate level of staffing to ensure high quality care is delivered with no consequent variation in mortality in hours or out of hours. Studies that do not demonstrate any increased odds of mortality during out of hours ICU admissions may relate to the fact that intensive care services are able to get priority response from the rest of the hospital.

The heterogeneity in casemix and outcomes between the different studies in this analysis was evident by the significant variation in overall patient mortality, ranging from 4% to 44% (23, 25). Whilst each study has adjusted the mortality risk for illness severity, the variables used to adjust and the case mix were different between studies. Differences in casemix, intensity of physician staffing (2, 6, 49, 50), intensivist grade (43), nursing staff to patient ratio (7) and 'closed' intensive care units (1) are organizational factors that may explain differences in patient outcome between different studies.

There is also likely to be significant variation in healthcare delivery between the various countries reporting data. Only 11 of the 16 studies included in our meta-analysis included information on intensivist staffing overnight. Therefore the effect of variation in staffing patterns among other organisational elements cannot be assessed. Studies adjust for differences in mortality using different illness severity scores, and the case mix in the different studies is variable. Twelve studies report hospital mortality (either in isolation or in addition to ICU mortality) whilst four studies report ICU mortality only. We also acknowledge that there was variation in definitions of night-time and weekend between studies.

Our findings of an increased odds of death among weekend admissions are consistent with a previous meta-analysis in 2010 (8). However, these results were largely attributable primarily one study that did not include analysis by time of day and accounted for 64% of the pooled odds ratio for mortality by day of week (9). In our up to date analysis, there are a further 7 studies with an additional 582,111 patients in the analysis by time of day and 656,860 patients in the analysis by day of week. A strength of our meta-analysis is the inclusion of more large trials, with no single trial having a dominant effect size.The major strength of our meta-analysis is the large sample sizes with 835,032 admissions analysed for effect of day of admission to intensive care and 717,331 patients included for analysis of time of admission to ICUs. Furthermore, we include a number of large studies, such that no single study has disproportionate weight.

The findings of this study, as with all meta-analyses, can only inform hypothesis testing. The data provided in this manuscript should be a prompt to investigate differences in health care organization and services between different countries. The challenge lies in trying to ascertain which differences are causal and which are merely associated with the different outcomes.

Conclusion

In conclusion, this meta-analysis shows an ‘out-of-hours’ effect with an associated increase in mortality with weekend ICU admissions compared to weekday admissions, but not with nighttime ICU admissions compared to daytime admissions. The increased mortality associated with weekend ICU admissions compared to weekday ICU admissions may be limited to North American countries and the absence of an on site intensivist. However, there is variation between definitions of ‘out of hours’ used, case mix, and staffing models, resulting in significant heterogeneity. Therefore caution needs to be used interpreting these results and changes to healthcare policy implemented.

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Figure Legends:

Figure 1a: Adjusted effect of nighttime admission to the ICU on mortality. Weight is the relative contribution of each study to the overall OR (random effects model with 95% CI).

Figure 1b: Adjusted effect of day of week admission to the ICU on mortality. Weight is the relative contribution of each study to the overall OR (random effects model with 95% CI).

Figure 2a: Adjusted effect of nighttime admission to the ICU on mortality by country of study. Weight is the relative contribution of each study to the overall OR (random effects model with 95% CI).

Figure 2b: Adjusted effect of nighttime admission to the ICU on mortality by country of study. Weight is the relative contribution of each study to the overall OR (random effects model with 95% CI).

Figure 3a: Adjusted effect of nighttime admission to the ICU on mortality by night time intensivist staffing. Weight is the relative contribution of each study to the overall OR (random effects model with 95% CI).

Figure 3b: Adjusted effect of nighttime admission to the ICU on mortality by night time intensivist staffing. Weight is the relative contribution of each study to the overall OR (random effects model with 95% CI).

Supplementary Figure: PRISMA flow chart with the number of studies evaluated at each stage of the systematic review

Fig 1a

Study or Subgroup	log[Odds Ratio]	SE	Night Total	Day Total	Weight	Odds Ratio IV, Random, 95% CI
Arulkumaran 2016	−0.01020077	0.00780238	122046	73382	12.8%	0.99 [0.97, 1.01]
Bhonagiri 2011	0.12139357	0.01014493	117073	127984	12.7%	1.13 [1.11, 1.15]
Brunot 2017	0.08190904	0.13406333	1462	966	3.8%	1.09 [0.83, 1.41]
Elkhayari 2014	0.3220835	0.34531848	70	125	0.8%	1.38 [0.70, 2.72]
Ju 2013	0.65232519	0.25243943	175	2716	1.4%	1.92 [1.17, 3.15]
Kuijsten 2010	0.05732507	0.01372779	42132	107762	12.6%	1.06 [1.03, 1.09]
Laupland 2008	0.31481074	0.04856052	8391	12075	9.8%	1.37 [1.25, 1.51]
Laupland 2011	−0.0618754	0.06788635	3855	3525	8.0%	0.94 [0.82, 1.07]
Lee 2008	−0.19845094	0.21206959	496	342	1.9%	0.82 [0.54, 1.24]
Meynaar 2009	0.11778304	0.07613908	2172	4553	7.3%	1.13 [0.97, 1.31]
Morales 2003	−0.46203546	0.0803793	3088	2946	7.0%	0.63 [0.54, 0.74]
Sheu 2007	0.37843644	0.19665059	297	314	2.1%	1.46 [0.99, 2.15]
Uusaro 2003	−0.02020271	0.07263821	14580	8554	7.6%	0.98 [0.85, 1.13]
Wunsch 2004	0.00990131	0.02054676	10772	45478	12.2%	1.01 [0.97, 1.05]
Total (95% CI)			**326609**	**390722**	**100.0%**	**1.04 [0.98, 1.11]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 195.38$, $df = 13$ ($P < 0.00001$); $I^2 = 93\%$

Test for overall effect: $Z = 1.35$ ($P = 0.18$)

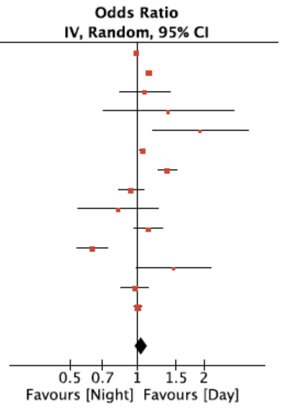


Fig 1b

Study or Subgroup	log[Odds Ratio]	SE	Weekend Total	Weekday Total	Weight	Odds Ratio IV, Random, 95% CI
Arulkumaran 2016	0	0.00911854	52387	143041	18.4%	1.00 [0.98, 1.02]
Barnett 2002	0.0861777	0.02564874	30579	76311	14.0%	1.09 [1.04, 1.15]
Bhonagiri 2011	0.03789144	0.01273867	49332	195725	17.6%	1.04 [1.01, 1.06]
Ensminger 2004	0.05543471	0.05347215	8108	20976	7.3%	1.06 [0.95, 1.17]
Kuijsten 2010	0.09803374	0.01503102	26893	123001	17.0%	1.10 [1.07, 1.14]
Laupland 2008	0.04879016	0.05313798	3680	16786	7.3%	1.05 [0.95, 1.17]
Laupland 2011	0.03580776	0.10827537	1708	5672	2.5%	1.04 [0.84, 1.28]
Lee 2008	0.0295588	0.26592778	248	590	0.5%	1.03 [0.61, 1.73]
Sheu 2007	−0.23572233	0.23375193	140	471	0.6%	0.79 [0.50, 1.25]
Uusaro 2003	0.18232156	0.08870676	4677	18457	3.5%	1.20 [1.01, 1.43]
Wunsch 2004	0.01152194	0.0344345	11345	44905	11.4%	1.01 [0.95, 1.08]
Total (95% CI)			**189097**	**645935**	**100.0%**	**1.05 [1.01, 1.09]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 41.07$, df = 10 ($P < 0.0001$); $I^2 = 76\%$
Test for overall effect: Z = 2.76 (P = 0.006)

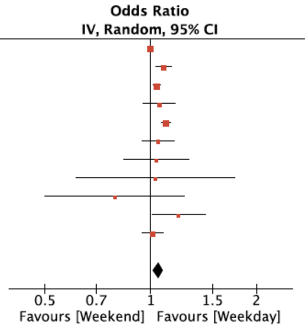


Fig 2a

Study or Subgroup	log[Odds Ratio]	SE	Night Total	Day Total	Weight	Odds Ratio IV, Random, 95% CI
13.1.1 North America						
Laupland 2008	0.31481074	0.04856052	8391	12075	9.8%	1.37 [1.25, 1.51]
Morales 2003	−0.46203546	0.0803793	3088	2946	7.0%	0.63 [0.54, 0.74]
Subtotal (95% CI)			**11479**	**15021**	**16.8%**	**0.93 [0.44, 1.99]**
Heterogeneity: $Tau^2 = 0.30$; $Chi^2 = 68.43$, df = 1 (P < 0.00001); $I^2 = 99\%$						
Test for overall effect: Z = 0.18 (P = 0.86)						
13.1.2 Europe						
Arulkumaran 2016	−0.01020077	0.00780238	122046	73382	12.8%	0.99 [0.97, 1.01]
Brunot 2017	0.08190904	0.13406333	1462	966	3.8%	1.09 [0.83, 1.41]
Kuijsten 2010	0.05732507	0.01372779	42132	107762	12.6%	1.06 [1.03, 1.09]
Laupland 2011	−0.0618754	0.06788635	3855	3525	8.0%	0.94 [0.82, 1.07]
Meynaar 2009	0.11778304	0.07613908	2172	4553	7.3%	1.13 [0.97, 1.31]
Usaro 2003	−0.02020271	0.07263821	14580	8554	7.6%	0.98 [0.85, 1.13]
Wunsch 2004	0.00990131	0.02054676	10772	45478	12.2%	1.01 [0.97, 1.05]
Subtotal (95% CI)			**197019**	**244220**	**64.3%**	**1.02 [0.98, 1.06]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 21.92$, df = 6 (P = 0.001); $I^2 = 73\%$						
Test for overall effect: Z = 0.89 (P = 0.38)						
13.1.3 Asia						
Ju 2013	0.65232519	0.25243943	175	2716	1.4%	1.92 [1.17, 3.15]
Lee 2008	−0.19845094	0.21206959	496	342	1.9%	0.82 [0.54, 1.24]
Sheu 2007	0.37843644	0.19665059	297	314	2.1%	1.46 [0.99, 2.15]
Subtotal (95% CI)			**968**	**3372**	**5.4%**	**1.31 [0.81, 2.11]**
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 7.44$, df = 2 (P = 0.02); $I^2 = 73\%$						
Test for overall effect: Z = 1.09 (P = 0.28)						
13.1.4 Australia						
Bhongari 2011	0.12139357	0.01014493	117073	127984	12.7%	1.13 [1.11, 1.15]
Subtotal (95% CI)			**117073**	**127984**	**12.7%**	**1.13 [1.11, 1.15]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 11.97 (P < 0.00001)						
13.1.5 Other countries						
Elkhayari 2014	0.3220835	0.34531848	70	125	0.8%	1.38 [0.70, 2.72]
Subtotal (95% CI)			**70**	**125**	**0.8%**	**1.38 [0.70, 2.72]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.93 (P = 0.35)						
Total (95% CI)			**326609**	**390722**	**100.0%**	**1.04 [0.98, 1.11]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 195.38$, df = 13 (P < 0.00001); $I^2 = 93\%$						
Test for overall effect: Z = 1.35 (P = 0.18)						
Test for subgroup differences: $Chi^2 = 22.71$, df = 4 (P = 0.0001), $I^2 = 82.4\%$						

Odds Ratio
IV, Random, 95% CI

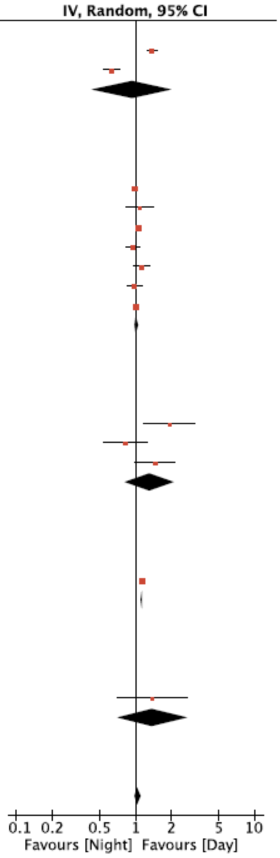


Fig 3a

Study or Subgroup	log[Odds Ratio]	SE	Night Total	Day Total	Weight	Odds Ratio IV, Random, 95% CI
11.1.1 Intensivist present						
Brunot 2017	0.08190904	0.13406333	1462	966	3.8%	1.09 [0.83, 1.41]
Laupland 2008	0.31481074	0.04856052	8391	12075	9.8%	1.37 [1.25, 1.51]
Laupland 2011	−0.0618754	0.06788635	3855	3525	8.0%	0.94 [0.82, 1.07]
Lee 2008	−0.19845094	0.21206959	496	342	1.9%	0.82 [0.54, 1.24]
Morales 2003	−0.46203546	0.0803793	3088	2946	7.0%	0.63 [0.54, 0.74]
Subtotal (95% CI)			**17292**	**19854**	**30.6%**	**0.94 [0.68, 1.30]**
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 74.43$, df = 4 ($P < 0.00001$); $I^2 = 95\%$						
Test for overall effect: Z = 0.36 (P = 0.72)						
11.1.2 No intensivist present						
Elkhayari 2014	0.3220835	0.34531848	70	125	0.8%	1.38 [0.70, 2.72]
Ju 2013	0.65232519	0.25243943	175	2716	1.4%	1.92 [1.17, 3.15]
Kuijsten 2010	0.05732507	0.01372779	42132	107762	12.6%	1.06 [1.03, 1.09]
Meynaar 2009	0.11778304	0.07613908	2172	4553	7.3%	1.13 [0.97, 1.31]
Sheu 2007	0.37843644	0.19665059	297	314	2.1%	1.46 [0.99, 2.15]
Usaro 2003	−0.02020271	0.07263821	14580	8554	7.6%	0.98 [0.85, 1.13]
Subtotal (95% CI)			**59426**	**124024**	**31.8%**	**1.11 [1.00, 1.23]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 10.54$, df = 5 (P = 0.06); $I^2 = 53\%$						
Test for overall effect: Z = 1.92 (P = 0.05)						
11.1.3 Intensivist presence not stated						
Arulkumaran 2016	−0.01020077	0.00780238	122046	73382	12.8%	0.99 [0.97, 1.01]
Bhongari 2011	0.12139357	0.01014493	117073	127984	12.7%	1.13 [1.11, 1.15]
Wunsch 2004	0.00990131	0.02054676	10772	45478	12.2%	1.01 [0.97, 1.05]
Subtotal (95% CI)			**249891**	**246844**	**37.6%**	**1.04 [0.95, 1.14]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 107.53$, df = 2 ($P < 0.00001$); $I^2 = 98\%$						
Test for overall effect: Z = 0.84 (P = 0.40)						
Total (95% CI)			**326609**	**390722**	**100.0%**	**1.04 [0.98, 1.11]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 195.38$, df = 13 ($P < 0.00001$); $I^2 = 93\%$						
Test for overall effect: Z = 1.35 (P = 0.18)						
Test for subgroup differences: $Chi^2 = 1.34$, df = 2 (P = 0.51), $I^2 = 0\%$						

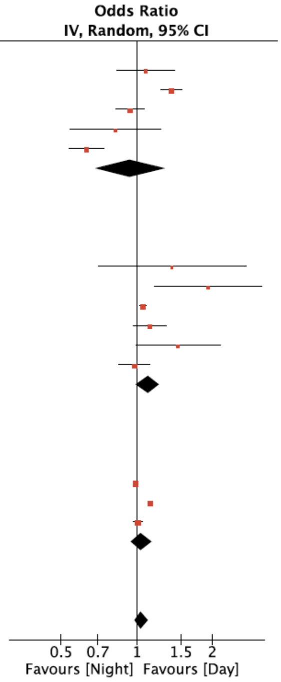
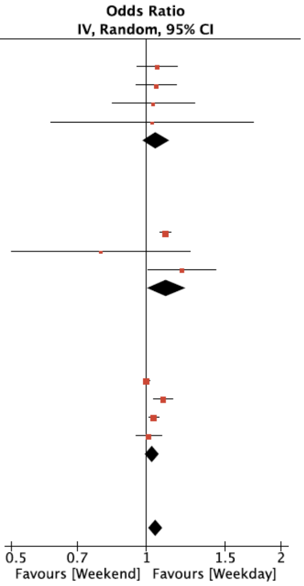


Fig 3b

Study or Subgroup	log[Odds Ratio]	SE	Weekend Total	Weekday Total	Weight	Odds Ratio IV, Random, 95% CI
10.1.1 Intensivist present						
Ensminger 2004	0.05543471	0.05347215	8108	20976	7.3%	1.06 [0.95, 1.17]
Laupland 2008	0.04879016	0.05313798	3680	16786	7.3%	1.05 [0.95, 1.17]
Laupland 2011	0.03580776	0.10827537	1708	5672	2.5%	1.04 [0.84, 1.28]
Lee 2008	0.0295588	0.26592778	248	590	0.5%	1.03 [0.61, 1.73]
Subtotal (95% CI)			**13744**	**44024**	**17.5%**	**1.05 [0.98, 1.13]**
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 3 (P = 1.00); I² = 0%						
Test for overall effect: Z = 1.42 (P = 0.16)						
10.1.2 No intensivist present						
Kuijsten 2010	0.09803374	0.01503102	26893	123001	17.0%	1.10 [1.07, 1.14]
Sheu 2007	−0.23572233	0.23375193	140	471	0.6%	0.79 [0.50, 1.25]
Usaro 2003	0.18232156	0.08870676	4677	18457	3.5%	1.20 [1.01, 1.43]
Subtotal (95% CI)			**31710**	**141929**	**21.1%**	**1.11 [1.00, 1.22]**
Heterogeneity: Tau² = 0.00; Chi² = 2.94, df = 2 (P = 0.23); I² = 32%						
Test for overall effect: Z = 2.02 (P = 0.04)						
10.1.3 Intensivist presence not stated						
Arulkumaran 2016	0	0.00911854	52387	143041	18.4%	1.00 [0.98, 1.02]
Barnett 2002	0.0861777	0.02564874	30579	76311	14.0%	1.09 [1.04, 1.15]
Bhongari 2011	0.03789144	0.01273867	49332	195725	17.6%	1.04 [1.01, 1.06]
Wunsch 2004	0.01152194	0.0344345	11345	44905	11.4%	1.01 [0.95, 1.08]
Subtotal (95% CI)			**143643**	**459982**	**61.4%**	**1.03 [1.00, 1.07]**
Heterogeneity: Tau² = 0.00; Chi² = 13.44, df = 3 (P = 0.004); I² = 78%						
Test for overall effect: Z = 1.74 (P = 0.08)						
Total (95% CI)			**189097**	**645935**	**100.0%**	**1.05 [1.01, 1.09]**
Heterogeneity: Tau² = 0.00; Chi² = 41.07, df = 10 (P < 0.0001); I² = 76%						
Test for overall effect: Z = 2.76 (P = 0.006)						
Test for subgroup differences: Chi² = 1.83, df = 2 (P = 0.40), I² = 0%						



Supl Fig 1

Figure 1- PRISMA diagram