Advances in Bioscience and Clinical Medicine
ISSN: 2203-1413
www.abcmed.aiac.org.au

Systematic Review and Meta-Analysis

Factors Associated with Prolonged Length of Stay in Intensive Care Unit: Systematic Review and Meta-analysis

Nashwa M. Radwan[1]*, MSc, MD, Nagla E. Mahmoud[2], MD, FFPH, Amal H. Alfaifi[3], SBFM, ABFM, Khaled I. Alabdulkareem[4], SBFM, ABFM

[1]*Professor of Public Health and Community Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt. Public Health consultant in Assisting Deputyship for Primary Health Care, Ministry of Health, Kingdom of Saudi Arabia*

[2]*Community Medicine specialist in Assisting Deputyship for Primary Health Care, Ministry of Health, Kingdom of Saudi Arabia*

[3]*Family Medicine specialist in Assisting Deputyship for Primary Health Care, Ministry of Health, Kingdom of Saudi Arabia*

[4]*Assistant professor of Family Medicine, College of Medicine, Al-Imam Mohammad Ibn Saud Islamic University (IMSIU), Kingdom of Saudi Arabia. Assistant Deputy Minister for Primary Health Care, Ministry of Health, Kingdom of Saudi Arabia*

Corresponding Author: Nashwa M. Radwan, E-mail: Radwan.n.m@gmail.com

ARTICLE INFO

Article history
Received: December 08, 2020
Accepted: December 05, 2020
Published: January 31, 2021
Volume: 9 Issue: 1

Conflicts of interest: All authors declare that no conflicts of interest with publication of the manuscript.
Funding: This research did not receive any specific grant from funding agencies.

Key words:
Prolonged Length of Stay,
Risk Factors,
Extended Length of Stay,
Patients,
Intensive Care Unit

ABSTRACT

Background: Prolonged length of Stay (PLOS) increases the risk of hospital-acquired infections and disrupts patient flow and access to care due to bed shortages. The extent to which PLOS is attributable to complications, patient characteristics, illness, or inefficien practice style is unclear. **Objectives:** To determine risk factors associated with prolonged length of stay (PLOS) in intensive care unit. (ICU). **Search methods:** We searched the COCHRANE, MEDLINE, TRIP and EMBASE from 2010 till now. **Selection criteria:** We included all the studies published in English language from 2010 till now and investigated the PLOS in ICU after any medical condition. **Data collection and analysis:** Two authors independently assessed trials eligibility and risk of bias and extracted data. Review Manager 5.3 was utilized to manage the data. **Main results:** The review included 84719 participants from fourteen observational studies that had some degree of risk of bias and substantial heterogeneity. Post-operative sepsis/ septic shock and the severity of illness of the patients at hospital admission were the most common risk factors for PLOS (OR= 5.65, CI= 1.98, 16.08 and OR=3.95, CI= 1.67, 9.34 respectively), followed by emergency operation (OR= 2.68, CI= 1.56, 4.62), and comorbidities including renal failure and coronary heart disease (OR= 2.64, CI=1.26, 5.51 and OR=2.57, CI= 1.61, 4.10 respectively). Other variables associated with PLOS were respectively; pre-operative condition (OR=2.36, CI=1.28, 4.34), long term use of corticosteroids (OR= 2.03, CI= 1.81, 2.29), age >70 years (OR=1.89, CI=0.54, 2.32), operation duration >180 minutes (OR=1.86, CI=1.46, 2.38), most deprived condition (OR= 1.82, CI= 1.15, 2.89), diabetes (OR= 1.36, CI=1.18, 1.56), hypertension (OR=1.32, CI= 1.09, 1.62), smoking (OR=1.25, CI= 1.13, 1.39) and male sex (OR= 1.11, CI=1.06, 1.17). **Authors conclusion:** Identification of risk factors associated with PLOS provides the opportunity for intervention to reduce the LOS and support efficient/optima use of hospital resources.

BACKGROUND

One of the most important factors that influence health management is the length of stay (LOS) in the intensive care unit (ICU) (1). It attracts the attention of healthcare systems as one of the major determinants of hospital cost and as an indicator of quality of care (2). PLOS not only delays patient discharge with higher costs due to increased use of medical resources, but it also predicts greater risk for readmission (3,4)

The definition of a prolonged ICU stay varies by hospital type, ICU type, and different diseases (5-9). Previous studies have shown factors associated with PLOS in ICU including; patient socio-demographic characteristics, higher comorbidity burden, provider characteristics, operative, intraoperative, postoperative variables, (10-15) and hospital administrative system factors e.g. delays in investigation and procedures [36] as well as the day and time of admission (16, 17) and low hospital workload (18).

A better understanding of the extent to which PLOS is attributable to patient illness, complications, or practice style difference is essential to develop interventions to reduce resource consumption and enhance quality of care. In this context, this systematic review and meta-analysis aimed

Published by Australian International Academic Centre PTY.LTD.
Copyright (c) the author(s). This is an open access article under CC BY license (https://creativecommons.org/licenses/by/4.0/)
http://dx.doi.org/10.7575/aiac.abcmed.v.9n.1p.30

to investigate factors associated with PLOS in ICU among patients with different medical conditions

Objective

This review aimed to assess the risk factors associated with PLOS in ICU after any medical condition.

METHODS

Criteria for Considering Studies for this Review

We included all available studied that investigated factors associated with PLOS in ICU following any medical condition and published in English language from 2010 till now.

Type of Participants

Patients admitted to ICU following any medical condition.

Exclusion Criteria

Infected patients in the isolation ward, Patients temporarily readmitted to intermediate ICU, individuals with a negative LOS (due to errors in dates recorded) and patients who died during hospital stay.

Outcome Measures

The outcome measures are the different variables associated with PLOS. The literature varies in defining the period at which a stay is considered as prolonged. PLOS is defined as LOS $\geq 90^{th}$ percentile (19, 20, 21, 22) or $\geq 75^{th}$ percentile (10, 23, 24, 25) or above the median LOS (14, 26) for the entire cohort of population. The different variables associated with PLOS will include; (1) patients' demographics (age, sex, smoking), (2) patients' presenting conditions at admission including comorbidities and severity of illness Severity of illness was measured using the Severity of Illness Rating Scale (SIRS) (27) based on patient symptoms, vital signs and categorised as low, moderate or high. Finally, (3) operative factors including; (a) Preoperative functional status measured by the American Society of Anaesthesiologists (ASA) class codes, which is an exhaustive list of surgical procedures ranked by complexity in ascending order [14, 28], (b) intraoperative factors including; operation type e.g. emergency or elective and operation duration, which is the time interval between incision to closure, (c) postoperative factors e.g. septic shock/ sepsis.

Search Methods for Identification of Studies

We systematically searched the following database; Cochrane Library, EMBASE, TRIP and MEDLINE through using the following terms; Length of stay, OR Prolonged length of stay, OR Extended length of stay, OR Intensive care unit stay, and Risk factors, OR Factors associated, OR Factors predicting, OR Clinical factors. The reference lists of the primary studied were also checked for additional studies.

Data Collection and Analysis

Selection of studies

Two authors independently read the titles and abstracts of potential articles. Relevant articles were obtained and read independently for inclusion criteria.

Data extraction and management

Two authors independently extracted the study characteristics from the included studies. One author transferred the data into the Review Manager (RevMan) 5.3 software (29)

Assessment of risk of bias in included studies

The potential risk of bias for each study was assessed independently by two authors and graded as high, low, or unclear according to the criteria of NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE for CASE CONTROL/ COHORT STUDIES in META-ANALYSIS (30). The scale utilised the following domains:

1- Adequate case definition (selection bias
2- Consecutive representativeness of cases (selection bias)
3- Selection of community controls (selection bias)
4- Adequate definition of controls (selection bias
5- Ascertainment of exposure/ independent blind assessment of outcome (selection bias)
6- Comparability of cases and controls on the basis of the design or analysis (comparability bias)
7- Same method of ascertainment for cases and controls/ Adequacy of follow up period (exposure/outcome bias)
8- All subjects complete follow up period/ Same response rate for both groups (exposure/outcome bias)

Assessment of quality of evidence

GRADE approach (Grading of Recommendations, Assessment, Development and Evaluation) (31) was used to assess quality of evidence based on four domains; risk of bias in the included studies, directness of the evidence, consistency across studies, and precision of the pooled estimate of outcome measure. The level of quality is judged on a four-point scale:

1- High quality: further research is very unlikely to change our confidence in the estimate of effect
2- Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate;
3- Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
4- Very low quality: the estimate of effect is very uncertain

Measures of treatment effec

Review Manager 5.3 (29) was utilized to manage the data using random effect model. Odds ratio and mean difference were used to present dichotomous and continuous data with 95% confidence interval.

Dealing with heterogeneity

I^2 statistic was used to measure heterogeneity among the included studies in each analysis (32).

RESULTS

Results of Search

We searched 174 potentially relevant articles, 102 were identified after removal of duplicates. Abstracts were reviewed independently by two authors based on inclusion and exclusion criteria. Twenty-one full-text articles were assessed for eligibility, of these, 14 met the inclusion criteria. Details of the search is given in the Prisma flow diagram (Figure 1).

Included Studies

Details of the study characteristics of the included studies (study design, duration of study, study setting, participants and outcome measures) are provided in Table 1 (supplementary appendix).

Trial Participants

The review included 84719 participants aged above 18 years of whom 19757 had PLOS. and 64962 had normal LOS. They were colorectal cancer surgery patients (Aravani et al,, Krell et al , Lobatoa et al, and Chiu et al,), ovarian cancer surgery patients (Smith et al), diabetic patients with severe hypoglycaemia (Chua et al), cardiac surgery patients (Almashrafi, et al, Mahesh et al, Eltheni et al, and Oliveira et al), acute stroke patients (Saxena et al), hepatobiliary and neurosurgery patients (Lee et al), trauma patients (Hwabejire et al) and very old patients >78 years (Toh et al).

Risk of Bias in included Studies

Overall, the studies included in this review were observational studies with some risk of bias. Independent assessment of outcome measures was high risk among two studies (Almashrafi et al and Chua et al), low risk among three (Lee et al, Saxena et al and and Toh et al) and unclear for the remaining studies. The same response rate for both cases and controls was high risk among two studies (Aravani et al and Toh et al), unclear in two studies (Lobatoa et al and Mahesh et al) and low in the remaining studies. Adequacy of follow up period was unclear in four studies (Chua et al, Eltheni et al, Lee et al and Mahesh et al) and low risk in the remaining studies. Consecutive cases representativeness was unclear risk among three studies (Lobatoa et al, Oliveira et al and saxena et al) and low risk in the remaining studies (Figure 2).

Outcome Measures

The association between patients' demographic characteristics and PLOS is explained in figures 3.1- 3.4 in the supplementary appendix. Age was a statistically significan factor with patients aged >70 years were about two folds of increased risk for PLOS (OR=1.89, CI= 1.54, 2.32), with significant considerable heterogeneity across the trials (I^2 =81%, P=0.0003). Also, male sex and smoking were sta-

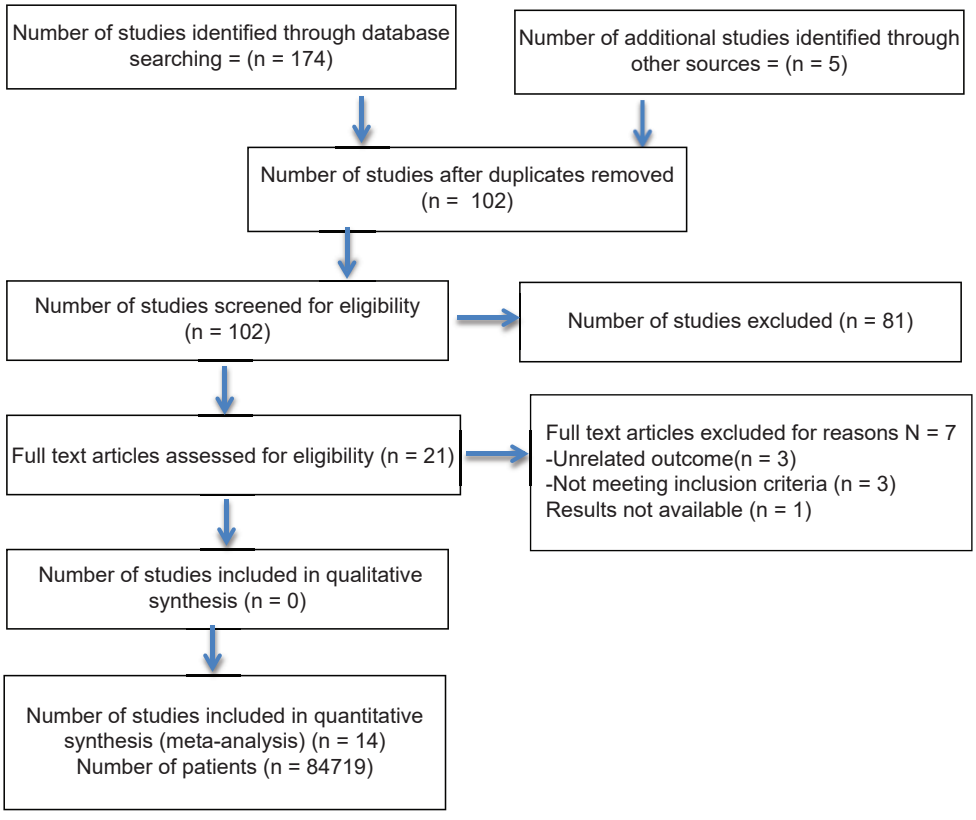

Figure 1. Prisma flow diagram

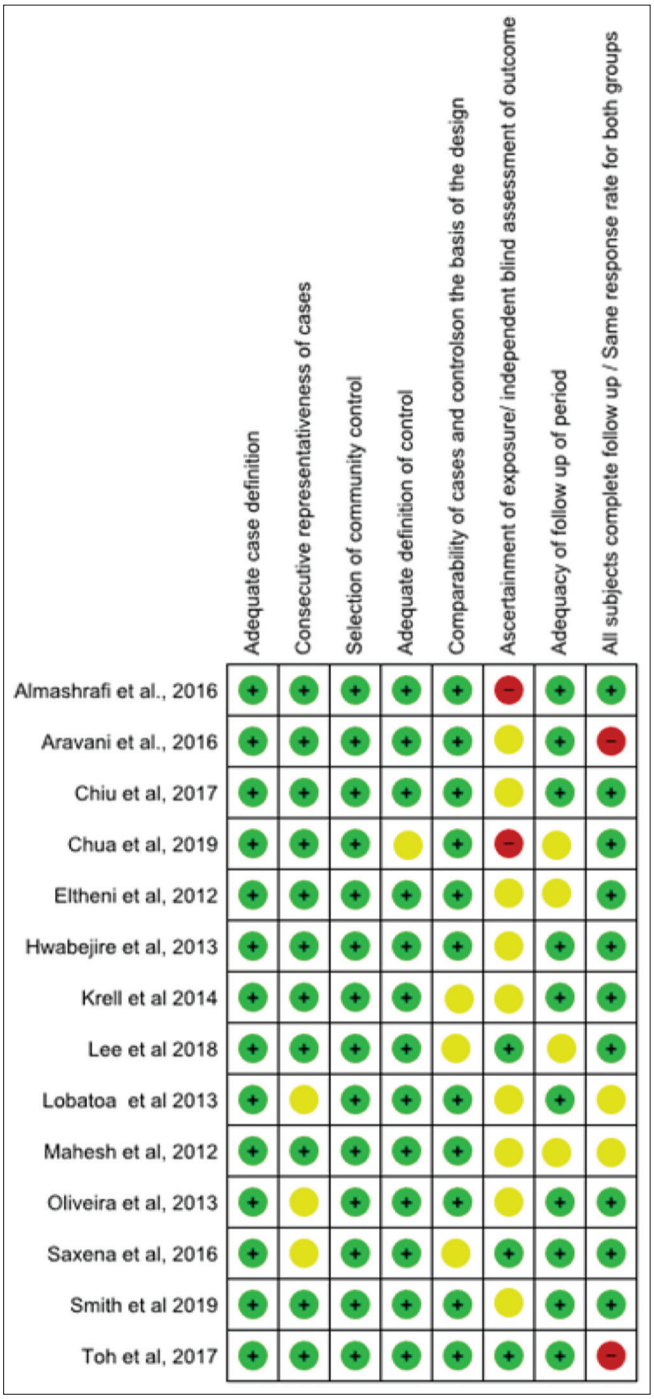

Figure 2. Risk of bias graph presented as percentages across all included studies according to authors' judgements about each item.

tistically significant factors for increasing the risk for PLOS (OR=1.11, CI= 1.06, 1.17 and OR=1.25, CI= 1.13, 1.39 respectively). Low insignificant heterogeneity was recorded in both analysis (I^2 =20%, and I^2 =0%, P<0.0001 respectively). A significant association between PLOS and economic deprivation (OR= 1.82, CI= 1.15, 2.89) was recorded in two studies with mild insignificant heterogeneity (I2 = 50%, P=0.16).

The condition of the patients at hospital admission was a significant factor affecting PLOS (Figures 4.1- 4.8 in supplementary appendix). Patients with high SIR scale were at about four folds of increased risk for PLOS (OR =3.95, CI=1.67, 9.34)., while those with low and moderate SIR had no significant increased risk (OR=0.43, CI=0.12, 1.56). The presence of diabetes and hypertension increased the risk for PLOS by about 1.5-fold (OR= 1.36, CI=1.18, 1.56, OR=1.32, CI= 1.09, 1.62 respectively). The risk increased to about 2.5 folds among patients with Coronary Heart Disease (CHD) and Renal Failure (RF) (OR=2.57, CI=1.61, 4.10 and OR= 2.64, CI= 1.26, 5.51 respectively), while the association of Chronic Obstructive Pulmonary Disease (COPD) and high Body Mass Index (BMI) was not a significant factor (OR= 1.24, CI= 0.61, 2.52 and OR= 1.03,CI= 0.81, 1.32 respectively). Significant considerable heterogeneity ranging from 63% to 100%, P<0.0001 was recorded, indicating inconsistency across the included studies, which could be explained by participants variation in demographic variables and type of medical condition at admission.

Pre-operative, operative, and post-operative variables affecting PLOS were explained in Figures 5.1-5.5 in sup-plementary appendix. A statistically significant association was recorded between PLOS and patients with grade 3,4 ASA classification, long-term use of corticosteroids, emer-gency operation, duration of operation >180 minutes and post-operative septic shock/ sepsis (OR= 2.36, CI= 1.28, 4.34 , OR= 2.03, CI= 1.81, 2.29 , OR= 2.68, CI=1.56, 4.62 , OR= 1.86, CI=1.46, 2.38 , and OR= 5.65, CI= 1.98, 16.08 respectively). Moderate to considerable heterogeneity was recorded across the trials (I^2 = 97%, 31%, 99%, 45% and 98%, P< 0.0001 respectively).

(Figure 5) Explains the forest plot of the pooled estimate of the significant risk factors for PLOS. Patients with post-operative sepsis/septic shock followed by those with high SIR scale represented the highest increased risk for PLOS (OR= 5.65, CI= 1.98, 16.08 and OR= 3.95, CI= 1.67, 9.34 respectively) compared to about 2- 2.5 folds of increased risk among patients aged >70 years, CHD, RF, ASA grade 3,4, long term corticosteroids use, emergency operation and operation duration >180 minutes (OR= 1.89, CI= 0.54, 2.32, OR=2.57, CI= 1.61, 4.10, OR= 2.64, CI= 1.26, 5.51, OR= 2.36, CI= 1.28, 4.34, OR= 2.03, CI= 1.81, 2.29, OR= 2.68, CI= 1.56, 4.62 and OR= 1.86, CI= 1.46, 2.38 respectively).

DISCUSSION

Summary of the Main Results

This review investigated the various factors associated with PLOS in ICU among 84719 participants in fourteen trials. Post-operative sepsis/ septic shock followed by the severity of illness of the patients at hospital admission were the most common risk factors for PLOS followed by emergency operation and underlying comorbidities including renal failure and coronary heart disease. Other factors associated with PLOS included; pre-operative physical status (ASA grade 3, 4), long term use of corticosteroids, age >70 years, operation duration >180 minutes, diabetes, hypertension, smoking and male sex.

Table 1. Quality of evidence of risk factors for PLOS

Outcome	Number of participants	OR	CI	Heterogeneity I^2, P	Quality of evidence
Age>70 years	43142	1.89	0.54, 2.32	81%, 0.0003	Low
Male sex	82948	1.11	1.06, 1.17	20%, <0.0001	Moderate
Smoking	13352	1.25	1.13, 1.39	0%, 0.48	Moderate
High SIR	72926	3.95	1.67, 9.34	99%, 0.002	Low
Diabetes	47125	1.36	1.18, 1.56	63%, <0.0001	Low
Hypertension	24311	1.32	1.09, 1.62	76%, 0.0003	Low
CHD	45250	2.57	1.61, 4.10	94%, 0.0001	Low
RF	28263	2.64	1.26, 5.51	93%, <0.0001	Low
ASA	20956	2.36	1.28, 4.34	97%, <0.0001	Low
Corticosteroids	35107	2.03	1.81, 2.29	31%, 0.23	Moderate
Emergency Operation	80324	2.68	1.56, 4.62	99%, <0.00001	Low
Duration of operation	3833	1.86	1.46, 2.38	45%, 0.12	Moderate
Post -operative sepsis	37037	5.65	1.98, 16.08	98%, 0.00001	Very low

SIR: severity of illness rating scale, CHD: coronary heart disease, RF: renal failure, ASA: American Society of Anaesthesiologists classification 3, 4,

Quality of Evidence

Overall, the studies included in this review were observational studies with considerable risk of bias, which downgraded the quality of evidence by one level for all outcome measures. Directness was not an issue as all included studies investigated the same outcome measure directly. We judged the quality of evidence to be moderate for the pooled estimate of the association between PLOS and male sex, smoking, long-term use of corticosteroids and operation duration >180 minute. We downgraded the evidence by one level only due to the observational designs of the included studies. Imprecision, directness, and heterogeneity were not significant issues (I^2 = 20%, 0%, 31% and 45% respectively). Regarding the pooled estimate of the association between PLOS and the following outcome; age>70 years, high SIR scale, diabetes, hypertension, CHD, RF, ASA classification 3,4, and emergency operation, we judged the quality of evidence to be low. Imprecision and directness were not significant issues, we downgraded the evidence by two levels due to observational designs of included studies besides considerable heterogeneity recorded in the analysis (I^2 = 81%, 99%, 63%76%, 94%, 93%, 97% and 99% respectively). For the pooled estimate of post- operative septic shock/ sepsis, we judged the quality of evidence to be very low. We downgraded the evidence by one more level because of some degree of imprecision indicated by wide confidence interval (CI= 1.98, 16.08) due to few studies included in the analysis. The considerable heterogeneity demonstrated in some analysis of the outcome measures, could be explained by differences among participants regarding socio-demographic characteristics, medical conditions at hospital admissions and cut off point for PLOS.

Overall Completeness and Applicability of Evidence

All studies included in our review recruited ICU patients with PLOS and were compared with those with regular LOS. Most of the included studies reported the sociodemographic characteristics of the participants and comorbidities except economic condition which was reported in two studies only. The severity of illness was recorded in eight studies. Operative variables including the type and the duration of operation were recorded in seven and five studies respectively and sepsis and ASA classification were investigated in four studies and three studies respectively.

Potential Biases in the Review Process

We systematically searched major databases and the reference lists of the primary studied were also checked. Two authors independently conducted all screening and data extraction. It is unlikely that the methods used in the review could have introduced bias.

Agreements and Disagreements with Other Studies or Reviews

Steady with our results, Almashrafi et al, 2016 (33) conducted a systematic review and investigated factors associated with increased LOS in ICU after cardiac surgery and recorded increased age, atrial fibrillation/ arrhythmia, chronic obstructive pulmonary disease (COPD), renal failure and non-elective surgery status.

Also, Walędziak et al, 2019 (34), Garza et al, 2018 (35), Kelly et al, 2012 (10), Cocker et al, 2011 (36), Herman et al, 2009 (37) and Ghotkar et al, 2006 (38) identified socio-demographic risk factors for PLOS including; older age (OR= 2.08, CI= 1.32, 3.26, OR=2.83, CI= 2.13-3.76, OR= 1.18, CI=1.02, 1.35, OR= 2.0, CI=1.5, 2.6 and OR= 2.20, CI= 1.40–3.46 respectively), male sex in Walędziak et al (34) and Garza et al 2018 (35) (OR= 0.63, CI= 0.40, 0.99 and OR= 1.08, CI= 1.05, 1.10 respectively), and smoking in Ghotkar et al (38) (OR= 1.6, CI=1.2, 2.0). This was consistent with our results (OR=1.89, CI=1.54, 2.32 for those aged >70 years and OR= 2.64, CI= 1.26, 5.51 for smoking). While Chan et al, 2014 (39) found that gender

Figure 3. (3.1-3.4) The association of demographic variables and PLOS

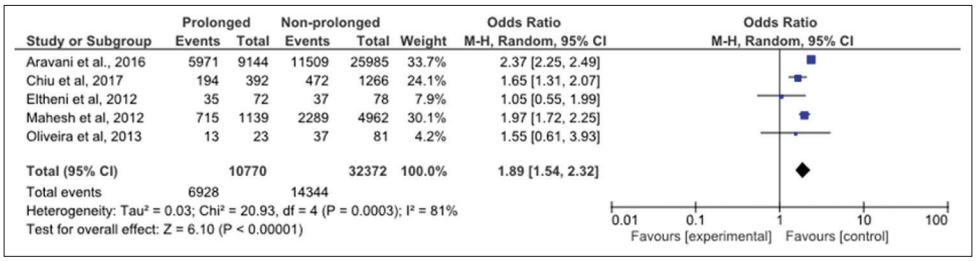

Figure 3.1. Forest plot of patients aged >70 years old and PLOS

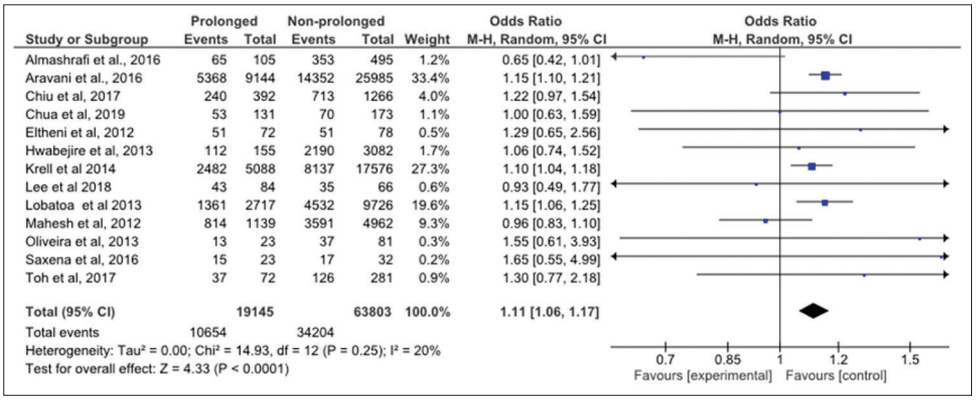

Figure 3.2. Forest plot of male sex and PLOS

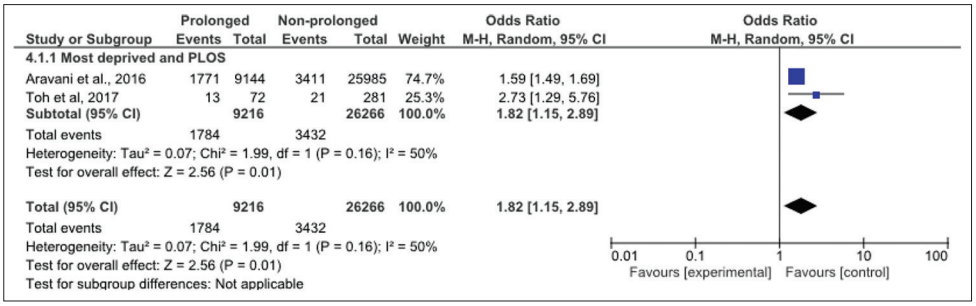

Figure 3.3. Forest plot of the most deprivation and PLOS among included trials.

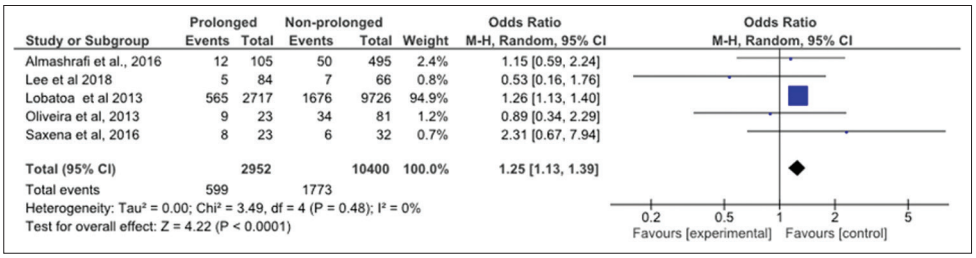

Figure 3.4. Forest plot of current smokers and PLOS among included studies

was not a significant factor. In addition, Kelly et al, 2012 (10) stated that deprived economic condition increased the risk for PLOS by about 1.5-fold (OR=1.42, CI= 1.16-1.75) which is nearly the same reported by the current review (OR= 1,82, CI= 1.15, 2.89).

Concerning underlying comorbidities among ICU patients, Kelly et al, 2012 (10) and Chan et al, 2014 (39) stated that comorbidities were significant risk factors for PLOS (OR= 2.46, CI=1.83-3.31 and OR= 1.715, CI=1.360, 2.161respectively). Walędziak et al 2019 (34), Cocker et al, 2011 (36), Herman et al, 2009 (37) and Ghotkar et al, 2006 (38) identified these comorbidities as CHD in Herman et al, 2009 (37)(OR= 1.37, CI= 1.01, 1.85) and RF in Cocker et al, 2011 (36), Herman et al, 2009 (37) and Ghotkar et al, 2006 (38) (OR= 1.24, CI= 1.10, 1.40, OR= 2.40, CI= 1.63–3.54, OR= 7.1, CI= 4.8, 10.5 respectively), diabetes in Walędziak et al, 2019 (34), Ghotkar et, 2006 (38) and Chan et al, 2014 (39) (OR= 3.24, CI= 1.46, 7.20 and OR= 1.9, CI= 1.5,

Figure 4. (4.1-4.8) Forest plot of severity of illness and comorbidity and PLOS

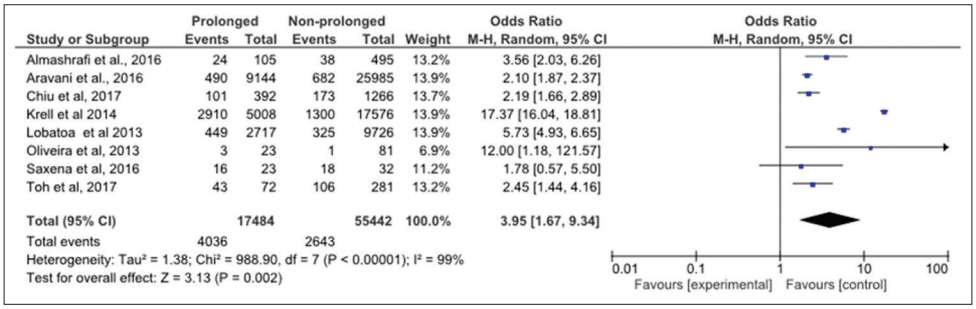

Figure 4.1. Forest plot of high severity of illness rating scale and PLOS

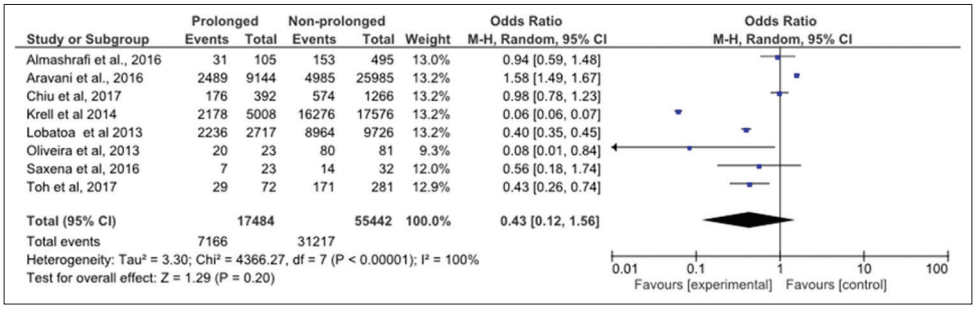

Figure 4.2. Forest plot of low and moderate severity of illness rating scale and PLOS

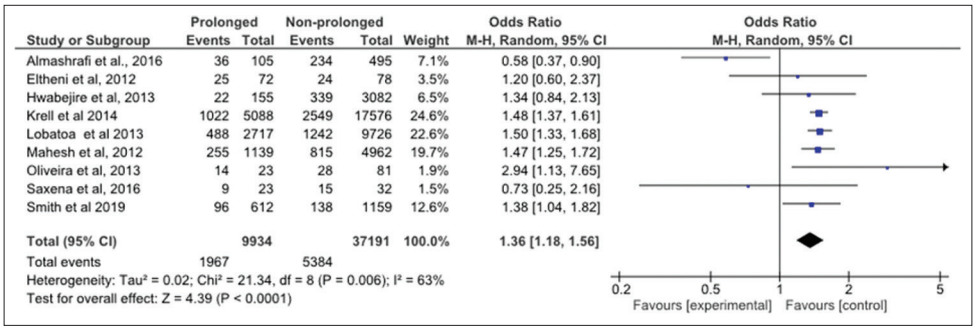

Figure 4.3. Forest plot of diabetes and PLOS

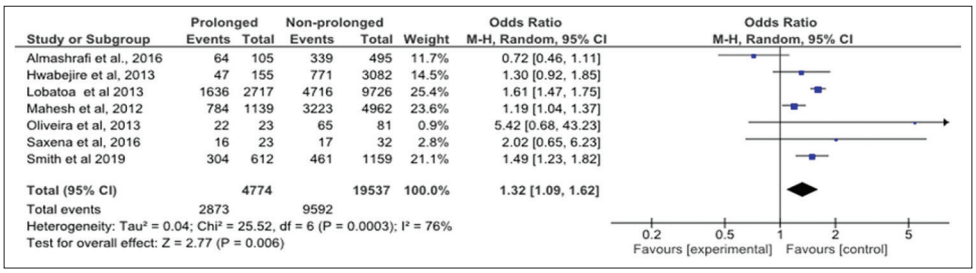

Figure 4.4. Forest plot of hypertension and PLOS

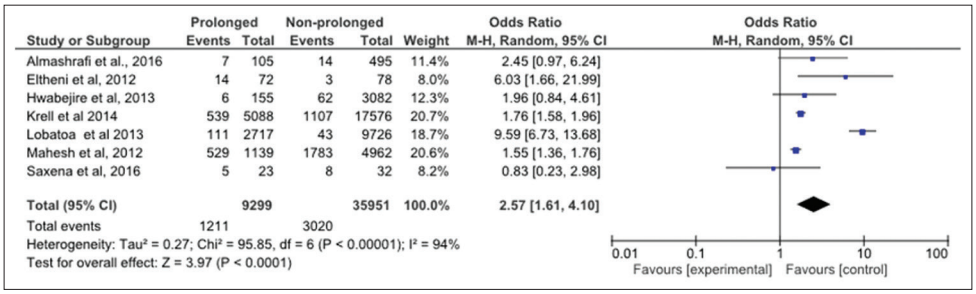

Figure 4.5. Forest plot of CHD and PLOS

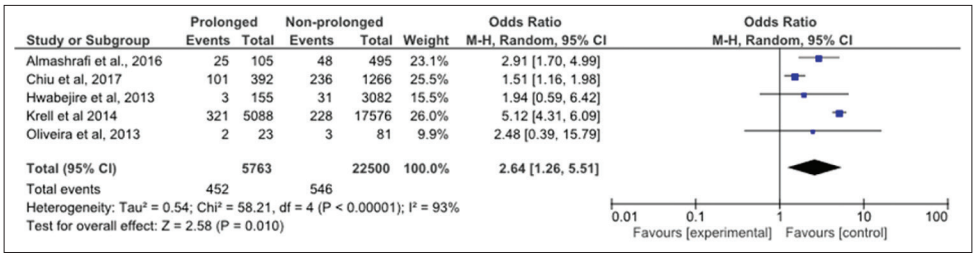

Figure 4.6. Forest plot of renal failure and PLOS

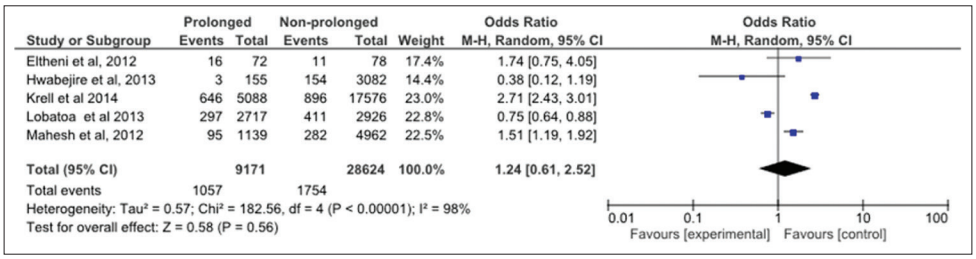

Figure 4.7. Forest plot of COPD and PLOS

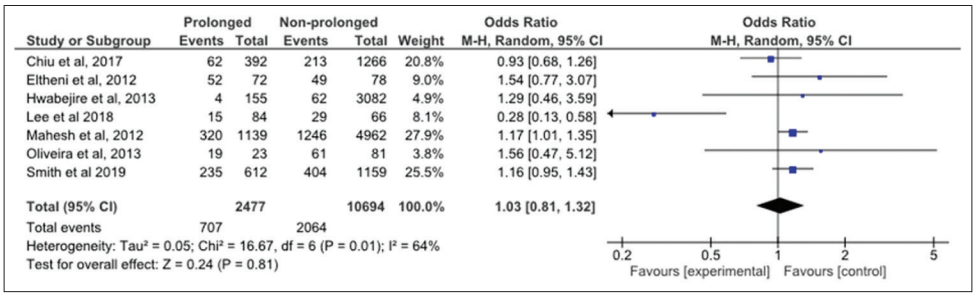

Figure 4.8. Forest plot of BMI and PLOS

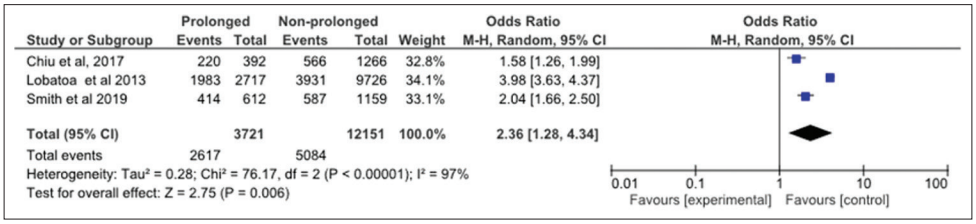

Figure 5.1. Forest plot of ASA classification 3, 4 and PLO

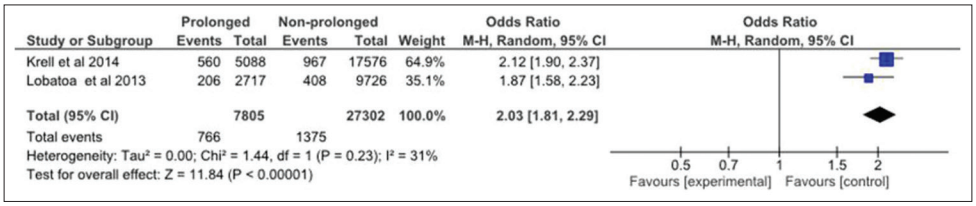

Figure 5.2. Forest plot of long-term corticosteroid use and PLOS

2.3 and OR= 4.918, CI= 3.764, 6.426 respectively), and hypertension in Ghotkar et al, 2006 (38) (OR= 1.5, CI=1.2, 1.8). This was consistent with our study for CHD, Rf, diabetes and hypertension (OR=2.57, CI=1.61, 4.10, OR= 2.64, CI= 1.26, 5.51, OR= 1.36, CI=1.18, 1.56 and OR=1.32, CI= 1.09, 1.62 respectively). While Our study recorded no significant association between obesity and PLOS (OR= 1.03, CI= 0.81, 1.32) which was inconsistent with Ghotkar et al, 2006 (38) (OR= 1.9, CI=1.3, 2.7) and could be explained by variation in method of identification and measurement of obesity between the different studies

In the present study, it was found that patients with high severity of illness at hospital admission are at about four folds of increased risk for PLOS (OR =3.95, CI=1.67, 9.34) and those with ASA classifica ion 3, 4 at about 2.5 folds (OR= 2.36, CI= 1.28, 4.34) which was nearly the same reported by Choi et al, 2017 (40) (OR= 3.297, CI=1.324, 10.483). Also, Cocker et al, 2011 (36) stated that ICU

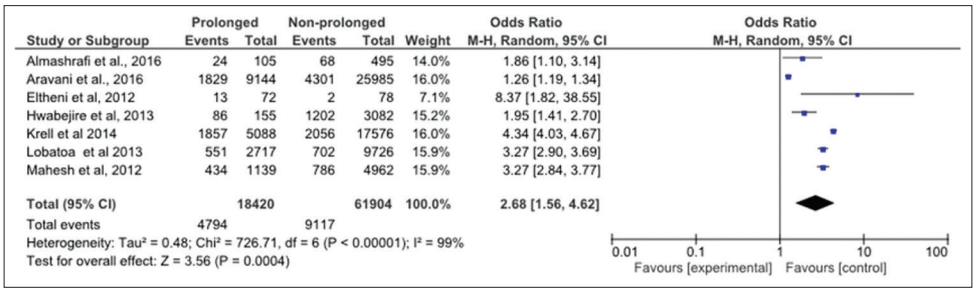

Figure 5.3. Forest plot of emergency operation and PLOS

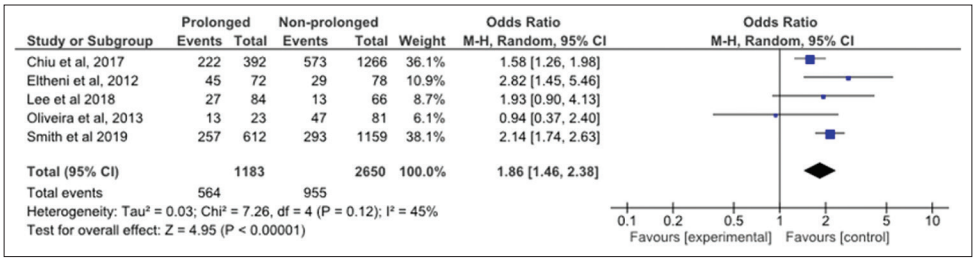

Figure 5.4. Forest plot of duration of operation >180 mint and PLOS

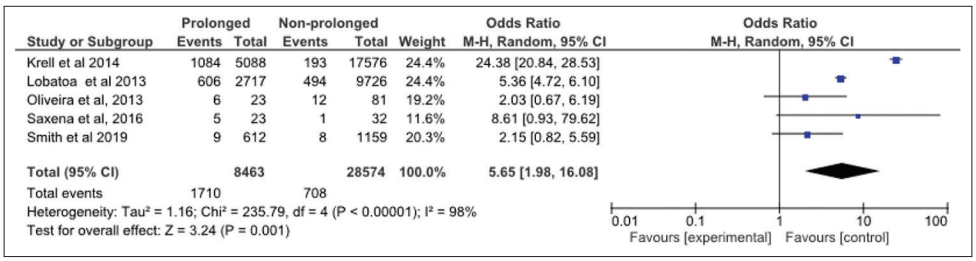

Figure 5.5. Forest plot of septic shock and PLOS

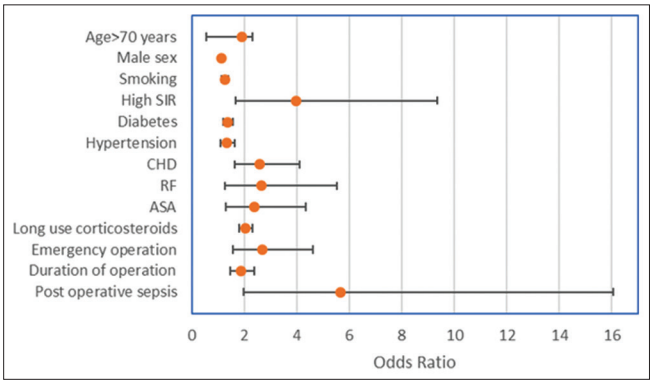

Figure 6. Forest plot of the pooled effect of the significant ris factors for PLOS. PLOS: prolonged length of stay

patients with unstable severe symptoms are at a significant risk for PLOS (OR= 1.142, CI= 1.025, 1.272).

The current review recorded operative risk factors for PLOS as emergent operation (OR= 2.68, CI=1.56, 4.62) and operation duration >180 minutes (OR= 1.86, CI=1.46, 2.38) and post -operative septic shock/ sepsis (OR= 5.65, CI= 1.98, 16.08) which was consistent with Cocker et al, 2011 (36), Ghotkar et al, 2006 (38) and Herman et al, 2009 (37) and Garza et al, 2018 (35) who indicated increased risk for non -electing operation (OR= 1.22, CI= 1.03, 1.51, OR= 3.4, CI= 2.1, 5.2, OR= 5.39, CI= 3.46, 8.38 and OR= 1.80, CI= 1.73, 1.87 respectively). Similarly, Walędziak et al 2019 (34) found that increased operation time was a significant risk for PLOS (OR= 1.01, CI= 1.01–1.02) and Stein et al, 2016 (41) found that post-operative complications increased the risk for PLOS by about three folds (OR= 2.701, CI= 2.077, 3.512) and discharge to post-acute care facility increased the risk by about 3.5 folds (OR= 3.47, CI=2.47, 4.87).

CONCLUSION

Our review highlighted several factors that can aid in predicting the PLOS in ICU. Interventions which address these factors could reduce LOS, improve outcome of these patients, optimise resource allocation and reduce hospital costs.

REFERENCES

1. Gruenberg DA, Shelton W, Rose SL, Rutter AE, Socaris S, and McGee G. "Factors influencing length of stay in the intensive care unit, "The American Journal of Critical Care 2006; 15(5): 502–509.
2. Thungjaroenkul P, Cunmings GG, and Embleton A. "The impact of nurse staffin on hospital costs and patient length of stay: a systematic review," Nursing Economics 2007; 25 (5): 255–265.
3. Damle RN, Cherng NB, Flahive JM., et al. Clinical and

financial impact of hospital readmissions after colorectal resection: predictors, outcomes, and costs. Dis Colon Rectum 2014; 57: 1421–1429.
4. Dekker JW, Gooiker GA, Bastiaannet E., et al. Cause of death the first year after curative colorectal cancer surgery; a prolonged impact of the surgery in elderly colorectal cancer patients. Eur J Surg Oncol 2014; 40: 1481–1487.
5. Martin CM, Hill AD, Burns K, and Chen LM. "Characteristics and outcomes for critically ill patients with prolonged intensive care unit stays," Critical Care Medicine 2005; 33 (9):1922–1927.
6. Laupland KB, Kirkpatrick AW, Kortbeek JB, and Zuege DJ. "Long-term mortality outcome associated with prolonged admission to the ICU," Chest 2006; 129 (4): 954–959.
7. Trottier V, McKenney MG, Beninati M, Manning R, and Schulman CI. "Survival after prolonged length of stay in a trauma intensive care unit," Journal of Trauma—Injury, Infection and Critical Care 2007; 62 (1): 147–150.
8. Huang YC, Huang SJ, Tsauo jy, and Ko WJ. "Definition risk factors and outcome of prolonged surgical intensive care unit stay," Anaesthesia and Intensive Care 2010; 38 (3):500– 505.
9. Ettema RGA, Peelen LM, Kalkman CJ, Nierich AP, Moons KJM, and Schuurmans MJ. "Predicting prolonged intensive care unit stays in older cardiac surgery patients: a validation study," Intensive Care Medicine 2011;37 (9):1480–1487.
10. Kelly M, Sharp L, Dwane F, et al. Factors predicting hospital length-of-stay and readmission after colorectal resection: a population-based study of elective and emergency admissions. BMC Health Serv Res 2012; 12: 77.
11. Al-Refaie WB, Parsons HM, Habermann EB, et al. Operative outcomes beyond 30-day mortality: colorectal cancer surgery in oldest old. Ann Surg 2011; 253: 947–952.
12. Faiz O, Haji A, Burns E, et al. Hospital stay amongst patients undergoing major elective colorectal surgery: predicting prolonged stay and readmissions in NHS hospitals. Colorectal Dis 2011; 13: 816–822.
13. Morris AM, Baldwin LM, Matthews B, et al. Reoperation as a quality indicator in colorectal surgery: a population-based analysis. Ann Surg 2007; 245: 73–79.
14. Collins TC, Daley J, Henderson WH, et al. Risk factors for prolonged length of stay after major elective surgery. Ann Surg 1999; 230: 251–259.
15. Bo M, Fonte G, Pivaro F, et al. Prevalence of and factors associated with prolonged length of stay in older hospitalized medical patients. Geriatr Gerontol Int 2016; 16:314-21.
16. Lim SC, Doshi V, Castasus B, Lim JKH, Mamun K. Factors causing delay in discharge of elderly patients in an acute care hospital. Ann Acad Med Singap. 2006; 35(1):27–32.
17. Earnest A, Chen MIC, Seow E. Exploring if day and time of admission is associated with average length of stay among inpatients from a tertiary hospital in Singapore: an analytic study based on routine admission data. BMC Health Serv Res. 2006; 6:6.
18. Cohen ME, Bilimoria KY, Ko CY, et al. Variability in length of stay after colorectal surgery: assessment of 182 hospitals in the national surgical quality improvement program. Ann Surg 2009; 250:901–7.
19. International Statistical Classification of Diseases (ICD). http://www. who.int/classifications/icd/en/. Accessed on May 22, 2015.
20. Bucerius J, Gummert JF, Walther T, et al. Predictors of prolonged ICU stay after on-pump versus off-pum coronary artery bypass grafting. Intensive Care Med 2004;30: 88 –95.
21. Janssen DP, Noyez L, Wouters C, Brouwer RM. Preoperative prediction of prolonged stay in the intensive care unit for coronary bypass surgery. Eur J Cardiothorac Surg 2004;25: –7.
22. Lateef F. Long Stayers in restructured hospitals. In: Ministry of Health, Singapore. Available at: https://www.moh.gov.sg/content/moh_web/home/pressRoom/ Parliamentary_QA/2013/long-stayers-in-restructured-hospitals-.html. Accessed May 20, 2015.
23. Abbott AM, Parsons HM, Tuttle TM, et al. Short-term outcomes after combined colon and liver resection for synchronous colon cancer liver metastases: a population study. Ann Surg Oncol 2013; 20: 139–147.
24. Gohil R, Rishi M and Tan BH. Preoperative serum albumin and neutrophil lymphocyte ratio are associated with prolonged hospital stay following colorectal cancer surgery. Br J Med Med Res 2014; 4: 481–487.
25. Lobatoa LF, Ferreirab PCA, Wickc EC, Kirand RP, Remzid FH, Kaladyd MF and Vogeld JD. Risk factors for prolonged length of stay after colorectal surgery. J. Coloproctol. (Rio J.) vol.33 no.1 Rio de Janeiro Mar./Apr. 2013 https://doi.org/10.1590/S2237-93632013000100005
26. Morimoto Y, Mizuno H, Akamaru Y, et al. Predicting prolonged hospital stay after laparoscopic cholecystectomy. Asian J Endosc Surg. 2015; 8(3):289–95.
27. Horn SD, Horn RA. Reliability and validity of the Severity of Illness Index. Med Care 1986; 24:159-78.
28. Table of Surgical Procedures, Ministry of Health. Accessed 3 May 2016 from https://www.moh.gov.sg/content/dam/moh_web/Healthcare_Financing/ Medisave/TOSP%20Booklet%20with%20MSP%20(3%20Jan%202017).pdf. Accessed 26 Dec 2017.
29. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen; The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
30. Wells GA, Shea B, Connell DO, Peterson J, Welch V, Losos M and Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses 2019.
31. Guyatt GH1, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008 336: 924.
32. Higgins JPT, Thompson SG, Deeks JJ, et al. Measur-

ing inconsistency in meta analyses. BMJ 2003; 327: 557 560.
33. Almashrafi A, Elmontsri M and Aylin P. Systematic review of factors influencing length of stay in ICU after adult cardiac surgery. BMC Health Services Research 2016; 16:318 DOI 10.1186/s12913-016-1591-3
34. Walędziak M, Lasek A, Wysocki M, Su M, Bobowicz M, Myśliwiec P. et al. Risk factors for serious morbidity, prolonged length of stay and hospital readmission after laparoscopic appendectomy - results from Pol-LA (Polish Laparoscopic Appendectomy) multicenter large cohort study. Scientific Reports 2019; 9:14793 | https://doi.org/10.1038/s41598-019-51172-2
35. Garza BAM, Zamudio PFB, Herrero AG, Zuñiga AC, Vega YC, Stalnikowitz DK and Osornio JS. Risk factors associated with prolonged hospital length-of-stay: 18-year retrospective study of hospitalizations in a tertiary healthcare center in Mexico. PLOS ONE 2018; November 8|https://doi.org/10.1371/journal.pone.0207203
36. Cocker J, Messaoudi N, Stockman BA, Bossaert LL, and Rodrigus IER. Preoperative prediction of intensive care unit stay following cardiac surgery. European Journal of Cardio-thoracic Surgery 2011; 39: 60—67 www.elsevier.com/locate/ejcts
37. Herman C, Karolak W, Yip AM, Buth KJ, Hassan A and Le´gare JF. Predicting prolonged intensive care unit length of stay in patients undergoing coronary artery bypass surgery – development of an entirely preoperative scorecard. Interactive CardioVascular and Thoracic Surgery 2009; 9:654–658.
38. Ghotkar SV, Grayson AD, Fabri BM, Dihmis WC and Pullan DM. Preoperative Calculation of Risk for Prolonged Intensive Care Unit Stay Following Coronary Artery Bypass Grafting. J Cardiothorac Surg. 2006; 31; 1:14. doi: 10.1186/1749-8090-1-14.
39. Chan CL, Ting HW and Huang HT. Spontaneous Intracerebral Haemorrhage Patients: An Application with National Health Insurance Research Database BioMed Research International Volume 2014, Article ID 891725, 9 pages http://dx.doi.org/10.1155/2014/891725.
40. Choi SK, Kim CK, Jo DI, Lee MC, Kim JN, Choi HG, Shin DH and Kim SH. Factors Associated with a Prolonged Length of Hospital Stay in Patients with Diabetic Foot: A Single-Center Retrospective Study. Arch Plast Surg 2017; 44:539-544 https://doi.org/10.5999/aps.2017.01207.
41. Stein M, Misselwitz B, Hamann GF, Kolodziej MA, Reinges MH and Eberhard U Defining Prolonged Length of Acute Care Stay for Surgically and Conservatively Treated Patients with Spontaneous Intracerebral Haemorrhage: A Population-Based Analysis. BioMed Research International Volume 2016, Article ID 9095263, 6 pages http://dx.doi.org/10.1155/2016/9095263

SUPPLEMENTARY

Table 1. Characteristics of included studies

Author	ID	Design	Setting	Aim	Participants	Outcome
1-Aravani et al., 2016	A retrospective observational study of length of stay in hospital after colorectal cancer surgery in England (1998–2010)	retrospective observational study	National Health Service (NHS) hospitals in England	To identify factors that significantly influence both optimal and prolonged LOS after colorectal cancer surgery	35129 individuals who underwent major resection for colorectal cancer between 1998-2010	Ideal LOS: 4.9% in 1998 to 34.2% in 2010, prolonged LOS: 11.2% to 8.4%, respectively.
2-Smith et al 2019	Clinical Factors Associated with Longer Hospital Stay Following Ovarian Cancer Surgery	Cohort study	The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database	to identify factors contributing to prolonged LOS for women undergoing surgery for ovarian cancer	women from 2012–2016 who underwent hysterectomy for ovarian, fallopian tube and peritoneal cancer.	factors associated with PLOS included: (ASA) Classification III or IV, presence of ascites, older age
3- Krell et al 2014	Extended Length of Stay After Surgery Complications, Inefficient Practice, or Sick Patients?	retrospective cohort study performed from January 1 through December 31, 2009,	2009 American College of Surgeons National Surgical Quality Improvement Program.	To examine the influence of complications on the variance in hospitals' extended LOS rates after colorectal resections.	22 664 adults (10619 males and 12045 females) undergoing colorectal resections in 199 hospitals.	wide variation in risk-adjusted extended LOS (14.5%-35.3%) and risk-adjusted inpatient complication (12.1%-28.5%) rates
4-Toh et al, 2017	Factors associated with prolonged length of stay in older patients	Retrospective study	Department of Geriatric Medicine at Khoo Teck Puat Hospital, Singapore from January 2013 to March 2013,	to investigate the factors associated with prolonged LOS among older patients (aged ≥ 78 years) in a tertiary hospital	72 PLOS patients and 281 non-PLOS patients	Caregiver stress and nursing home placement are potential modifiable risk factors of PLOS
5- Chua et al 2019	Factors associated with prolonged length of stay in patients admitted with severe hypoglycaemia to a tertiary care hospital	retrospective cohort study	Singapore General Hospital (SGH) from January 2014 and January 2015	To elucidate factors associated with PLOS among patients with severe hypoglycaemia.	304 diabetic patients with mean age of 70.6 ± 11.3 years	Patients with PLOS had significantly higher Charlson Comorbidity index (CCI) (4.9 ± 2.1 vs 4.1 ± 2.1, P < 0.01)
6- Almashrafi, et al., 2016	Factors associated with prolonged length of stay following cardiac surgery	Retrospective observational study	A major referral hospital in Oman between 2009 and 2013.	to identify factors influencing prolonged postoperative length of stay (LOS) following cardiac surgery.	All adult patients underwent cardiac surgery at a major referral hospital in Oman	30.5% of the patients had PLOS (≥11 days) after surgery, while 17% experienced prolonged ICU LOS (≥5 days
7 -Saxena et al, 2016	Factors Predicting Length of Hospital Stay in Acute Stroke Patients Admitted in a Rural Tertiary Care Hospital	A hospital based prospective study	Mahatma Gandhi Institute of Medical Sciences, Sevagram in central India. between April 1, 2014 and July 31, 2014	to determine factors that extend the LOS in hospital of acute stroke patients.	55 stroke patients 32 males and 23 females.	PLOS in stroke patients was related to location of lesions and low Glasgow coma scale scores

(*Contd...*)

Table 1. (*Continued*)

Author	ID	Design	Setting	Aim	Participants	Outcome
8- Mahesh et al, 2012	Prolonged Stay in Intensive Care Unit Is a Powerful Predictor of Adverse Outcomes After Cardiac Operations	Retrospective observational study	Papworth Hospital, Cambridgeshire, United Kingdom; From January 2003 to December 2007,	to examine the impact of prolonged intensive care unit (ICU) stay on in-hospital mortality and long-term survival.	6101 consecutive patients underwent cardiac operations and 1,139 patients had a PLOS	18.7% patients had PLOS had a higher ICU mortality (10%) compared with controls
9- Lobatoa et al, 2013	Risk factors for prolonged length of stay after colorectal surgery	Retrospective study	2007 American-College-of-Surgeons-National-Surgical-Quality-Improvement-Program (ACS-NSQIP) database	to identify factors associated with PLOS after colorectal surgery.	2,617 (21.3%) patients underwent colorectal operations with PLOS	Risk factors for prolonged LOS were male gender, congestive heart failure, weight loss, Crohn's disease,
10- Eltheni et al, 2012	Predictors of Prolonged Stay in the Intensive Care Unit following Cardiac Surgery	An observational cohort study	A tertiary hospital of Athens, Greece from September 2010 to January 2011.	to identify preoperative and intraoperative predictors for PLOS	150 consecutive patients, for cardiac surgery ICU	AF and renal dysfunction, and hyperglycaemia are significant risk factors for PLOS
11- Lee et al 2018	Factors associated with prolonged length of stay for elective hepatobiliary and neurosurgery patients: a retrospective medical record review	A retrospective cross-sectional medical record review study	A 1250-bed tertiary academic hospital in Singapore from January 2014 to January 2015	to explore perioperative factors associated with PLOS for elective HPB and NS patients to improve safety and quality of practice.	All elective HPB (150) and NS (166) patients over 18 years old	preoperative factors had the greatest association with PLOS for HPB and NS elective surgeries
12- Chiu et al, 2017	The impact of complications on prolonged length of hospital stay after resection in colorectal cancer: A retrospective study of Taiwanese patients	A retrospective study	Two medical centres; Kaohsiung Medical University Hospital, Kaohsiung, and E-DA Hospital, Kaohsiung, in southern Taiwan between 2005–2010	To assess the impact of minor, major and individual complications on prolonged length of hospital stay in patients with colorectal cancer (CRC) after surgery	1658 patients who underwent surgery for stage I–III CRC	Minor and major complications were significantly associated with PLOS
13- Hwabejire et al, 2013	Excessively Long Hospital Stays After Trauma Are Not Related to the Severity of Illness Let's Aim to the Right Target!	A retrospective study	Massachusetts General Hospital Level I academic trauma centre. From January 1, 2006, and December 31, 2010.	To identify the causes of excessively prolonged hospitalization (ExProH) in trauma patients.	3237 adult trauma patients	Of 3237 patients, 155 (5%) had Extended PLOS. were older, likely to have blunt trauma, more likely to be self-payers
14- Oliveira et al, 2013	Risk factors for prolonged hospital stay after isolated coronary artery bypass grafting	A case-control study	In 2007 at the Instituto de Cardiologia do Distrito Federal hospital (IC-DF)	to evaluate individual and perioperative risk factors of prolonged hospitalization in intensive care units and wards.	104 patients who underwent isolated CABG with median age (extremes) of 60 (37-82)	Hospital stay >3 days in the intensive care unit occurred for 22.1% of patients and >7 days in the ward for 27.9%.

REFERENCES

1. Aravani A, Samy EF, Thomas JD, Quirke P, Morris EJA, Paul J. and Finan PJ. A retrospective observational study of length of stay in hospital after colorectal cancer surgery in England (1998–2010) Medicine (2016) 95:47(e5064). http://dx.doi.org/10.1097/MD.0000000000005064
2. Smith CG, Davenport DL, Gorski J, McDowell A, Burgess BT, Tricia I. Fredericks TI., et al. Clinical Factors Associated with Longer Hospital Stay Following Ovarian Cancer Surgery. Healthcare 2019, 7, 85; doi:10.3390/healthcare7030085
3. Krell RW, Girotti ME and Dimick JB. Extended Length of Stay After Surgery. Complications, Inefficien Practice, or Sick Patients? JAMA Surg. 2014;149(8):815-820. doi:10.1001/jamasurg.2014.629
4. Toh HJ, Lim ZY, Yap P and Tang T. Factors associated with prolonged length of stay in older patients. Singapore Med J 2017; 58(3): 134-138 doi: 10.11622/smedj.2016158.
5. Chua JM, Lim W, Bee YM, Goh SY, Tick CEC, Xia HAT and et al. Factors associated with prolonged length of stay in patients admitted with severe hypoglycaemia to a tertiary care hospital. Endocrinol Diab Metab. 2019;2:e00062. | https://doi.org/10.1002/edm2.62
6. Almashrafi A, Alsabti H, Mukaddirov M, Balan B and Aylin P. Factors associated with prolonged length of stay following cardiac surgery in a major referral hospital in Oman: a retrospective observational study. BMJ Open 2016;6:e010764. doi:10.1136/bmjopen-2015-010764
7. Saxena A, Prasad RN, Verma K and Saxena S. Factors Predicting Length of Hospital Stay in Acute Stroke Patients Admitted in a Rural Tertiary Care Hospital J Gerontol Geriatr Res 2016, S5:003 DOI: 10.4172/2167-7182.S5-003
8. Mahesh B, Choong CK, Goldsmith K, Gerrard C, Nashef SAM and Vuylsteke A. Prolonged Stay in Intensive Care Unit Is a Powerful Predictor of Adverse Outcomes After Cardiac Operations. Ann Thorac Surg 2012; 94:109 –16
9. Lobatoa LF, Ferreirab PCA, Wickc EC, Kirand RP, Remzid FH, Kaladyd MF and Vogeld JD. Risk factors for prolonged length of stay after colorectal surgery J. Coloproctol. (Rio J.) vol.33 no.1 Rio de Janeiro Mar./Apr. 2013 https://doi.org/10.1590/S2237-93632013000100005
10. Eltheni R, Giakoumidakis K, Brokalaki H, Galanis P, Nenekidis and Fildissis G. Predictors of Prolonged Stay in the Intensive Care Unit following Cardiac Surgery. International Scholarly Research Network ISRN Nursing Volume 2012, Article ID 691561, 9 pages doi:10.5402/2012/691561
11. Lee1SY, Lee SH, Tan JHH, Foo HSL, Phan PH, Kow AWC, Lwin S, Seah PMY and Mordiffi SZ. Factors associated with prolonged length of stay for elective hepatobiliary and neurosurgery patients: a retrospective medical record review. BMC Health Services Research 2018, 18:5 DOI 10.1186/s12913-017-2817-8
12. Chiu HC, Lin YC, Hsieh HM, Chen HP, Wang HL and Wang JY et al. The impact of complications on prolonged length of hospital stay after resection in colorectal cancer: A retrospective study of Taiwanese patients. Journal of International Medical Research 2017, Vol. 45(2) 691–705 DOI: 10.1177/0300060516684087 journals.sagepub.com/home/imr
13. Hwabejire JO, Kaafarani HMA, Imam AM, Solis CV, Justin Verge J, Sullivan NM, DeMoya MA, Alam HB and Velmahos GC. Excessively Long Hospital Stays After Trauma Are Not Related to the Severity of Illness Let's Aim to the Right Target! JAMA Surg. 2013;148(10):956-961. doi:10.1001/jamasurg.2013.2148
14. Oliveira EK, Turquetto ALR, Tauil PL, Fernando L, Jr J and Porto LGG. Risk factors for prolonged hospital stay after isolated coronary artery bypass grafting. Rev Bras Cir Cardiovasc 2013;28(3):353-63 DOI: 10.5935/1678-9741.20130055