Advances in Patient Safety

Clinical and Economic Advantages of Continuous Respiratory Monitoring on the General Care Floor

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Improvement in patient safety encompasses a multitude of solutions. Continuous patient monitoring can make a significant difference in improving patient outcomes by delivering continuous visibility into a patient's health status by translating the data into potentially actionable interventions. The sooner a healthcare professional can recognize clinical deterioration or condition changes, the earlier the intervention.

Learning Objectives
After completing this activity, the participant will be able to:

1. Recognize signs and symptoms of patient deterioration.
2. Discuss the emergence of new technologies to predict early deterioration
3. Evaluate the cost effectiveness of implementing continuous respiratory monitoring on the GCF

Continuing Education (CME)
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Disclosures
The faculty and planners disclosed no conflicts of interest associated with this activity.

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Abstract

Unexpected adverse events resulting in transfer to the intensive care unit occur in up to 9% of hospitalized patients on the general care floor. Although there are several reasons for adverse events, early detection of patient deterioration can prevent patient morbidity and mortality as well as healthcare costs. Two of the most important components of early detection of patient deterioration are education of the healthcare team on signs and symptoms of deterioration, and the presence of quality wireless and wearable continuous monitoring that provides the ability of nurses to visualize patient change over time.

There are several methods for continuous electronic monitoring of respiratory status. Choosing the most patient-centric, sensitive, and feasible method is key in early detection of patient deterioration. Preferred patient-centric choices are the devices that the patient is more likely to comply with wearing.

Patients who experience an adverse respiratory event during hospitalization have higher hospital costs and longer lengths of stay that result in a higher incremental cost of complication of between $3,000 and $38,000 cost per patient stay. The implementation of continuous electronic monitoring of respiratory status of the hospitalized patient is slowly becoming a standard of care as opposed to 2- or 4-hour spot check of vital signs. There exists a potential for continuous monitoring of patients' respiratory status to have a significant economic benefit in addition to clinical benefits. In this age of healthcare reimbursement moving away from fee-for-service and towards value-based payments, decreasing adverse events with earlier detection of patient deterioration using continuous respiratory monitoring is essential.

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Significance of the problem of adverse events secondary to unidentified respiratory depression in the hospitalized patient

Unexpected adverse events resulting in transfer to the intensive care unit occur in up to 9% of hospitalized patients on the general care floor.[1-4] Although there are several reasons for adverse events, early detection of patient deterioration can prevent patient morbidity and mortality as well as healthcare costs.[5-9]. Specifically, Cardoso and colleagues found that each hour of delay in ICU admission of deteriorating patients was associated with a 1.5% increase in risk of death in the ICU and a 1% increase in mortality.[8] Two of the most important components of early detection of patient deterioration are education of the healthcare team on signs and symptoms of deterioration, and the presence of quality wireless and wearable continuous monitoring that provides the ability of nurses to visualize patient change over time. [10,11] Other components such as the use of the electronic medical record, deterioration scores or indexes, and safety alerts have also been found beneficial.[7,12] The best performing deterioration algorithms rely on accurate and frequent/continuous measurement of respiratory rate, pulse rate, blood pressure, and temperature.[13,14] In particular, many studies have found that accurate measurement of respiratory status is the most predictive of patient deterioration.[12, 15-20] It is important for members of the healthcare team as well as electronically-driven deterioration algorithms to recognize specific patterns of respiratory insufficiency and to continuously measure the parameters that are the most sensitive to change in respiratory status. Healthcare systems can no longer afford adverse events and unnecessary lengths of stay that will not be included in third party reimbursements.

> Early detection of patient deterioration on the general care floor leads to rapid targeted management and can help reduce the need for the patient to transfer to a higher level of care.

Early detection of patient deterioration on the general care floor leads to rapid targeted management and can help reduce the need for the patient to transfer to a higher level of care; thereby reducing hospital length of stay and cost while improving survival rates. [21,22] Rapid-response systems have been put in place world-wide to address critical illness outside the ICU in patients that have clinically deteriorated with the aim of preventing serious adverse events. [23] Most facilitates now have patient safety strategies such as rapid response teams that are responsive to the bedside nurses call for assistance in assessing a patient who is deteriorating. Rapid response systems are composed of an afferent limb that ensures identification of the patient who may be deteriorating, and an efferent arm, which is the response to the patient bedside. Numerous studies have been conducted in the United States and other countries that demonstrate failure of the afferent limb and the commonality of adverse events and their associated disability and death.[24-29] Abnormal vital signs have been shown in several studies to help identify clinical deterioration in patients for minutes to hours before the event occurs.[30,]

[31] Specifically, changes in respiratory rate has been found to be a 1) strong predictor of clinical outcomes, 2) one of the most sensitive markers of the condition of the patient and 3) can be the first sign of deterioration in a patient's condition.[32, 33] Respiratory rate is subject to assessment by multiple clinicians over the course of hospitalization and research has demonstrated low sensitivity in the detection of bradypnoea and tachypnoea with criterion standard measurements with spot assessment as opposed to continuous electronic monitoring. [33, 34] Continuous electronic monitoring along with astute interpretation of change in respiratory status over time of the hospitalized patient housed on the general care floor (GCF) will lead to earlier detection of clinical deterioration with subsequent earlier initiation of the rapid response system.

Measuring Respiratory Status: Oxygenation Versus Ventilation

There are five respiratory parameters that can be measured electronically on the general care floor. They are: respiratory rate (RR), oxygen saturation via pulse oximetry (PO), end tidal carbon dioxide via capnography (ETCO2), transcutaneous carbon dioxide (TCCO), and minute ventilation (MV). Electronic devices that measure each or a combination of these parameters are available and approved for clinical use. There are clinical indications for each parameter that reflect either a measure of ventilation or oxygenation. Ventilation is the process of exchange of air between the lungs and the ambient air. Oxygenation is the process of infusing blood with oxygen. Without ventilation, oxygenation cannot occur.

Measuring Ventilation

Respiratory rate. There are two ways of measuring respiratory rate, (1) visually counting breaths at one point in time, or (2) electronically via a device that is either measuring chest movement, air movement through mouth or nose, or the sound of breath.

Electronic acoustic respiratory rate monitoring has been found to reduce adverse events.

All these types of devices have been found valid in counting breaths per minute. Electronic acoustic respiratory rate monitoring has been found to reduce adverse events.[35] In studies of postoperative respiratory depression, oxygen desaturations occurred that were not detected by changes in respiratory rate.[36, 37] Pairing the respiratory rate monitor with pulse oximetry results in increased sensitivity for the detection of OIRD (opioid-induced respiratory depression). [38] Normal respiratory rate for adults <65 years ranges between 12-18 breaths per minute (BPM) during wakefulness and increases as high as 20 BPM during states of sleep or sedation. [39] Breathing in states of sleep or sedation should remain between 12-20 BPM in patients <60 years of age, 12-28 BPM between 65-80 years, and between 10-30 in patients >80 years of age.[40] Assessing respiratory rate should always involve comparison to the patient's baseline and change over time and is a more effective measure of respiratory insufficiency when combined with other measures of ventilation and oxygenation.[41]

Respiratory quality. Although continuous respiratory rate monitoring has been found to improve patient safety by aiding in early recognition of patient deterioration, nursing assessment of breathing is also very important. Electronic monitoring should never replace nursing assessments. The ability to assess respiratory quality requires attention to breathing patterns. When approaching a patient to measure respirations, clinicians should first visualize the depth, rhythm and rate of breathing. Tidal volume, represented by the depth of breath, decreases during sleep thus breathing may appear shallower. The rhythm of breathing during wakefulness should remain steady, but normal breathing rhythms during REM sleep may be irregular.[42] Medications that cause respiratory depression such as benzodiazepines and opioids will increase the normal collapsibility of the pharyngeal airway that occurs during sleep leading to a change in breathing pattern as well as possible audible snoring.[43] Snoring is the sign of a partially collapsed airway. A patient experiencing opioid or sedation induced respiratory depression may exhibit a respiratory rate below 12 BPM initially, but then as the body compensates, rates may increase to greater than 18 BPM. Additionally, tidal volume or depth of breath will be shallow, and rhythm will be irregular representing pharyngeal collapsibility/apneic events.[44, 45] Clinicians should use their auditory senses to listen for snoring, which is a sign of varying degrees of pharyngeal collapse.[46-48] A patient with sleep disordered breathing such as obstructive sleep apnea will likely exhibit noisy breathing and a distinct pattern with pause in breaths for more than 10 seconds, then a louder snore as they arouse to open their airway. [49] Because sleep states pose risks for pharyngeal collapsibility that may be increased with sedating agents and lack of voluntary control of breathing, it is important for clinicians to be extra vigilant and use continuous electronic monitoring when patients are sleeping to ensure patient safety. [50, 51] Electronically, quality of breath as well as respiratory rate can be measured using a Respiratory Volume Monitor (RVM).

Minute Ventilation. Minute ventilation (MV) is measured using a respiratory volume monitor (RVM). Minute ventilation is calculated using a measure of tidal volume (TV) and respiratory rate (RR). The RVM uses bio-impedance to provide real-time measurement of MV via electrodes placed at the sternal and mid-auxiliary placements. [52] Clinical studies have shown that monitoring MV is effective, comfortable for the patient, and in some cases more effective in detecting OIRD than measuring respiratory rate, oxygen saturation, or end tidal CO2. [53-57] Traditionally, the alarm is set at <40% of predicted/normal MV for more than 2 minutes. Possible issues with the measurement of MV include lack of detection of breath in obese patients, electrodes not adhering and delivering consistent and accurate readings due to chest wall hair. Limits patient mobility!

Capnography. Arterial carbon dioxide ($PaCO_2$) is the gold standard for measuring ventilation, but measuring $PaCO_2$ is invasive and not feasible for the general care floor. Capnography is a device that measures exhaled end tidal carbon dioxide (et CO_2) levels via a cannula positioned under the nasal nares and a scoop that sits over the upper portion of the mouth. End tidal carbon dioxide has been validated as an effective measure of respiratory status and can improve patient safety when administered opioids. [58, 59] Capnography is more effective in detecting respiratory depression compared to intermittent every 4-hour pulse oximetry assessments.[60] Other clinical studies have compared capnography to pulse oximetry and some have found capnography superior in detecting OIRD. [61-63] Barriers to the use of capnography on general care units are lack of nursing knowledge of the device plus interpreting CO_2 levels, cost, availability of equipment, and patient adherence. [64, 65] Normal values of end tidal CO_2 range 35 to 45 mmHg. Monitoring with capnography has been found to significantly reduce the incidence of OIRD with patient controlled analgesia (PCA) by 79% as measured by decreased rapid response team ($P<.001$) and rate of transfers to a higher level of care.[66]

Transcutaneous Carbon Dioxide.
A device that has more recently been converted for use in adults is transcutaneous carbon dioxide ($tcCO_2$). The device requires a sensor that is heated above body temperature and placed on the surface

An earlier indicator of hypoventilation is combining the measurement of respiratory rate with oxygen saturation or using other methods of measuring ventilation.

of the skin. Placement is usually on the earlobe, face, or chest. The heating of the sensor allows for local arterialization. The temperature of the sensor is usually 40°C and 44°C and set according to the skin location of the sensor.[54, 55 67, 68] In a meta-analysis by Conway et al, sensor placement and heat settings were compared and found that the earlobe placement with temperature set >42°C had a higher correlation with arterial $PaCO_2$ levels.[69] Research has shown that there are clinically relevant differences between $tcCO_2$ and arterial CO_2 in patients with poor perfusion. $TcCO_2$ has been validated against arterial PCO_2 and is effective in the detection of respiratory insufficiency when comparing individual changes over time. [70]

Summary. There are several methods for continuous electronic monitoring of respiratory status. Choosing the most patient-centric, sensitive, and feasible method is key in early detection of patient deterioration. Preferred patient-centric choices are the devices that the patient is more likely to comply with wearing. Devices such as capnography require a cannula that gets in the way of conversations, eating, and sleeping comfortably. Additionally, devices that tether the patient to the bed decrease the likelihood of compliance with wearing continuously and interfere with safe ambulation. Recognizing that measures of ventilation, as opposed to oxygenation, have higher sensitivity for measurement of respiratory status which, should play an important role in choosing the best device for the patient's conditions. Feasibility and availability are probably two of the most limiting factors. Most hospitals have limited availability to capnography, transcutaneous CO_2 devices, and minute ventilation on the general care floors. Additionally, nurses require significant training on these newer and more novel measures of ventilation, leaving the combination of oxygen saturation with respiratory rate monitoring the most accessible and feasible option. Hospitals must be committed to improved patient safety and add the devices and training to the budgets.

Measuring Oxygenation

Oxygen saturation. Pulse oximetry devices measure the percentage of hemoglobin bound with oxygen in arterial blood. Sites of measurement are usually the finger, ear lobe, toe, or lateral nares. Normal oxygen saturation levels range 95-100% while awake and >92% when asleep. Elderly patients may exhibit normal awake oxygen levels as low as 91%.[71] In general, an oxygen saturation of less than 90% for more than 15 seconds is considered clinically relevant. According to the American Academy of Sleep Medicine, repeated oxygen desaturations of 3% from baseline for greater than 10 seconds is clinically relevant and associated with poor health outcomes.[72] [59] There is sufficient research and expert consensus recommending the use of pulse oximetry to detect OIRD with opioid-based therapies following surgery. [62, 63] Continuous nocturnal pulse oximetry has been found to be a reliable screening procedure for detecting obstructive sleep apnea in patients not wearing supplemental oxygen.[78] In the hospital setting, the alarm threshold is usually set at <90% SpO_2, but some studies have found that a threshold of 88% may decrease alarm fatigue and be sensitive enough to avoid opioid related events. [79] The use of supplemental oxygen can blunt the accuracy of detecting respiratory depression when monitoring oxygen desaturation. [62, 80-83]

Summary. Although there are devices that measure just one parameter, research has found that measuring multiple parameters is more sensitive than one single parameter.[84] For example, patients are able to maintain near normal oxygen saturation for a period of time during clinically relevant hypoventilation. Thus, an earlier indicator of hypoventilation is combining the measurement of respiratory rate with oxygen saturation or using other methods of measuring ventilation. Other considerations for implementing continuous electronic monitoring on the general care floor are related to the development of hospital policies that empower nurses to initiate electronic monitoring using nursing judgement for patients at risk, staff education on the use of the monitoring devices and the underlying physiology of respiratory depression, as well as the interpretation of monitor waveforms and clinical data.

Pathophysiology of three main patterns of respiratory insufficiency in the hospitalized patient

There are three main patterns of respirations seen on the general care floor that are signs of respiratory insufficiency and patient deterioration; all are best detected by continuous electronic respiratory monitoring.

Pattern I is usually seen in sepsis, congestive heart failure, aspiration and/or pulmonary emboli. The physiology is the replacement of normal functional residual capacity (FRC) in or around the lungs with fluid, inflammatory or infectious factors. The respiratory parameter that is most affected is respiratory rate. Compensatory mechanisms will induce an increase in respiratory rate to compensate for the decrease in FRC. Pattern I will initially present with slowly increasing respiratory rate, then as the FRC fills with fluid or infectious material, the oxygen saturation will begin to fall and respiratory alkalosis will develop. During this phase, the patient may report some mild dyspnea and/or anxiety.

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Pattern II is typically seen with medication induced hypoventilation. The hypoventilation results in buildup of carbon dioxide. Escalation of hypoventilation, not responsive to rising carbon dioxide levels, will result in CO_2 necrosis, severe respiratory acidosis and respiratory arrest. Patients who are successfully compensating from medication induced hypoventilation will exhibit increasing respiratory rate that allows for increased exhalation of carbon dioxide. The use of continuous respiratory rate/ventilation monitoring is necessary to capture respiratory changes over time and ensures the patient experiences adequate compensation. Although most patient's natural respiratory drive will compensate to the depression of the central respiratory centers, there are up to 4% of hospitalized patients who receive opioids and are incapable of adequate compensation. Unfortunately, prediction and risk stratification of those patients is not always accurate, thus continuous monitoring of respiratory status is necessary to assure patient safety.

Pattern III occurs in patients with undiagnosed sleep apnea with slow arousal threshold.[85] Obstructive sleep apnea occurs as the result of collapsibility of the pharyngeal airway. During states of sleep or sedation, everyone experiences some level of pharyngeal collapsibility. In some patients with smaller, shorter, more crowded airways, the collapse limits airflow resulting in oxygen desaturation. Chemoreceptors will respond to decreasing SpO_2 by causing an arousal from sleep, thus resulting in an increase in pharyngeal muscle tone. Unfortunate for some patients, the arousal response is delayed resulting in dangerously low SpO_2 levels and retention of carbon dioxide. This situation is called impaired arousal threshold, and can result in respiratory arrest (found dead in bed) especially in the setting of opioid and other sedating medications. Without continuous monitoring, this condition is not often discovered. With continuous monitoring, the hospital health care team can become very frustrated with recurrent oxygen desaturation and respiratory rate alarms. The best treatment for this condition is positive airway pressure therapy and decreasing the amount of sedating medications, not ignoring or silencing the alarms.

Examine the cost implications for instituting best monitoring practices for monitoring respiratory status in the hospitalized patient

Patients who experience an adverse respiratory event during hospitalization have higher hospital costs and longer lengths of stay that result in a higher incremental cost of complication of between $3,000 and $38,000 cost per patient stay.[87-89] The implementation of continuous electronic monitoring of respiratory status of the hospitalized patient is slowly becoming a standard of care as opposed to 2- or 4-hour spot check of vital signs. There exists a potential for continuous monitoring of patients' respiratory status to have a significant economic benefit in addition to clinical benefits. In this age of healthcare reimbursement moving away from fee-for-service and towards value-based payments, decreasing adverse events with earlier detection of patient deterioration using continuous respiratory monitoring is essential.[90]

Unfortunately, instituting continuous monitoring requires significant cost related to the purchase of equipment and training of staff.[86] Defending the financial investment of implementing continuous respiratory monitoring devices into a standard of care on the general care floor requires careful investigation of the cost of care of the patient who has experienced deterioration or an adverse event. Intensive care unit cost and reimbursement has been studied extensively as they are considered to be the most expensive units within hospitals representing an estimated 27% of Medicare cost.[91] A substantial burden on the health care systems is placed by patients housed in ICUs with spending exceeding $80 billion per year, representing approximately 3% of all health care spending and nearly 1% of the US gross domestic product.[93] Many hospitals are admitting low risk of mortality patients to ICUs for cardiac or respiratory monitoring when continuous monitoring is not available on the general care floor.[94]

In a study conducted by McGrath and colleagues, wireless patient sensors and pulse oximetry-based surveillance system monitors with advanced display and information system capabilities were introduced to the GCF.[95] Data collection included patient characteristics, vital sign documentation, monitor alarm, workflow, and system utilization for a period of 5 months before and five months after system implementation with an accompanied staff satisfaction survey.[95] Comparison unit data for the same period was also collected and analyzed for the identical time period. 90 Statistical analysis to examine differences pre-and post-study for both target and control groups was performed and revealed a reduced average vital sign collection time of 28%, with an increase in patient monitoring time (rate ratio 1.22) and real-time accuracy of patient information.[95] This study was unique in that it was inclusive of a staff satisfaction survey with a 65% response rate and revealed overall system satisfaction ratings of 4 or 5 on the 5-point scale were 79% for Licensed Nurse Assistants and 78% for RN's.

Associated costs with continuous monitoring of patients on the GCF including hardware costs, hospital charges and fees need to be considered in any analysis of the benefits, however this has not been widely studied. Slight and colleagues conducted a 5-year return on investment study utilizing a monitoring unit which collected data and compared it to previous data during a 9-month period measuring heart rate, respiratory rate, and bed movement.[92] This study demonstrated savings between $3,268,000 (conservative model B, which was based on the cost of care on the last day of stay) and $9,089,000 (base model A which estimated the total cost savings on length of stay (LOS), ICU LOS, and treatment of pressure ulcers), given an 80% prospective reimbursement rate. The study reported a net benefit of between $2,687,000 ($658,000 annualized) and $8,508,000 ($2,085,000 annualized), with the hospital breaking even on the investment after 0.5 and 0.75 of a year, respectively. The average net benefit of implementing the system ranged from $224 per patient (model B) to $710 per patient (model A) per year.[92]

Studying the relationship between cost and improvement in patient outcomes has been found to be complex and may involve shifting the focus from volume to value. In a cost-effectiveness analysis involving continuous patient monitoring conducted at Dartmouth-Hitchcock Medical Center, expansion of patient surveillance through continuous monitoring found that cost-effectiveness depended upon the impact of patient surveillance. The model was based upon reduction of ICU transfers and days spent in the ICU. Implementation costs for a 36-bed unit amounted to $167,993,993, with a $58,261 annual cost.[96] Prior to the introduction of patient surveillance, the length of stay of a patient transferred from the ICU was 24.39 (7.67 days in

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ICU plus 16.72 days on the GCF) and afterwards the average LOS dropped to 19.32 days (3.87 days in the ICU plus 13.45 days on the GCF). This amounted to $1,479,012 for the initial study unit and influenced the ICU bed supply in terms of availability.[96] It should be noted that this study also included increased surveillance on a medical unit with no realization in decreased cost, but an increase in cost with no association in change in outcome. Cost savings may also be realized by refined algorithms which will allow for more patients to be cared for with fewer clinicians.[97]

Summary

The healthcare industry in general has accepted patient safety as a priority at every patient encounter. Patients are hospitalized as they are not safe to recover at home and expect that the healthcare team continuous presence while hospitalized will improve their chances of recovery. Unfortunately, adverse events continue to occur and most are characterized by respiratory deterioration. It is time for hospitals to recognize the benefits of continuous electronic (respiratory) monitoring in the early detection of patient deterioration. There is evidence that instituting electronic monitoring on the general care floor is cost effective, acceptable to the patient and hospital staff, and clinically effective.

References

1. de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. Qual Saf Health Care. 2008;17(3):216-23. doi: 10.1136/qshc.2007.023622. PubMed PMID: 18519629; PMCID: PMC2569153.
2. Dahn CM, Manasco AT, Breaud AH, et al. A critical analysis of unplanned ICU transfer within 48 hours from ED admission as a quality measure. *Am J Emerg Med*. 2016;34(8):1505-10. Epub 2016/05/11. doi: 10.1016/j.ajem.2016.05.009. PubMed PMID: 27241571.
3. Zhang E, Hung SC, Wu CH, Chen LL, Tsai MT, Lee WH. Adverse event and error of unexpected life-threatening events within 24hours of ED admission. *Am J Emerg Med*. 2017;35(3):479-83. Epub 2016/11/30. doi: 10.1016/j.ajem.2016.11.062. PubMed PMID: 27974226.
4. Vlayen A, Verelst S, Bekkering G, Schrooten W, Hellings J, Claes N. Incidence and preventability of adverse events requiring intensive care admission: a systematic review. *Journal of Evaluation in Clinical Practice*. 2012;18(2):485-97. doi: 10.1111/j.1365-2753.2010.01612.x. PubMed PMID: WOS:000301053800038.
5. Frost SA, Alexandrou E, Bogdanovski T, Salamonson Y, Parr MJ, Hillman KM. Unplanned admission to intensive care after emergency hospitalisation: risk factors and development of a nomogram for individualising risk. *Resuscitation*. 2009;80(2):224-30. *Epub* 2008/12/11. doi: 10.1016/j.resuscitation.2008.10.030. PubMed PMID: 19084319.
6. Schmidt PE, Meredith P, Prytherch DR, et al. Impact of introducing an electronic physiological surveillance system on hospital mortality. *BMJ Qual Saf*. 2015;24(1):10-20. Epub 2014/09/23. doi: 10.1136/bmjqs-2014-003073. PubMed PMID: 25249636.
7. Mathukia C, Fan W, Vadyak K, Biege C, Krishnamurthy M. Modified Early Warning System improves patient safety and clinical outcomes in an academic community hospital. *J Community Hosp Intern Med Perspect*. 2015;5(2):26716. Epub 2015/04/01. doi: 10.3402/jchimp.v5.26716. PubMed PMID: 25846353; PMCID: PMC4387337.
8. Cardoso L, Grion C, Matsuo T, et al. Impact of delayed admission to intensive care units on mortality of critically ill patients: a cohort study. *Critical Care*. 2011;15(1). doi: 10.1186/cc9975. PubMed PMID: WOS:000288961900028.
9. Vincent J, Einav S, Pearse R, et al. Improving detection of patient deterioration in the general hospital ward environment. *European Journal of Anaesthesiology*. 2018;35(5):325-33. doi: 10.1097/EJA.0000000000000798. PubMed PMID: WOS:000429440800001.
10. Hogan H, Carver C, Zipfel R, et al. Effectiveness of ways to improve detection and rescue of deteriorating patients. *Br J Hosp Med (Lond)*. 2017;78(3):150-9. doi: 10.12968/hmed.2017.78.3.150. PubMed PMID: 28277760.
11. Castaneda C, Nalley K, Mannion C, et al. Clinical decision support systems for improving diagnostic accuracy and achieving precision medicine. *Journal of Blinical Bioinformatics*. 2015;5(1):4-. doi: 10.1186/s13336-015-0019-3.
12. Hollis RH, Graham LA, Lazenby JP, et al. A Role for the Early Warning Score in Early Identification of Critical Postoperative Complications. *Ann Surg.* 2016;263(5):918-23. doi: 10.1097/SLA.0000000000001514. PubMed PMID: 26692076.
13. Bailey TC, Chen Y, Mao Y, et al. A trial of a real-time alert for clinical deterioration in patients hospitalized on general medical wards. *J Hosp Med*. 2013;8(5):236-42. Epub 2013/02/25. doi: 10.1002/jhm.2009. PubMed PMID: 23440923.
14. Churpek MM, Yuen TC, Huber MT, Park SY, Hall JB, Edelson DP. Predicting cardiac arrest on the wards: a nested case-control study. *Chest*. 2012;141(5):1170-6. Epub 2011/11/03. doi: 10.1378/chest.11-1301. PubMed PMID: 22052772; PMCID: PMC3342781.
15. Churpek MM, Yuen TC, Winslow C, Meltzer DO, Kattan MW, Edelson DP. Multicenter Comparison of Machine Learning Methods and Conventional Regression for Predicting Clinical Deterioration on the Wards. *Crit Care Med*. 2016;44(2):368-74. doi: 10.1097/CCM.0000000000001571. PubMed PMID: 26771782; PMCID: PMC4736499.
16. Verrillo SC, Winters BD. Review: Continuous Monitoring to Detect Failure to Rescue in Adult Postoperative Inpatients. *Biomed Instrum Technol*. 2018;52(4):281-7. doi: 10.2345/0899-8205-52.4.281. PubMed PMID: 30070913.
17. Farley H, Zubrow MT, Gies J, et al. Emergency department tachypnea predicts transfer to a higher level of care in the first 24 hours after ED admission. *Acad Emerg Med*. 2010;17(7):718-22. doi: 10.1111/j.1553-2712.2010.00796.x. PubMed PMID: 20653585.
18. Hosking J, Considine J, Sands N. Recognising clinical deterioration in emergency department patients. *Australas Emerg Nurs J*. 2014;17(2):59-67. Epub 2014/04/06. doi: 10.1016/j.aenj.2014.03.001. PubMed PMID: 24815204.
19. Buist M, Bernard S, Nguyen T, Moore G, Anderson J. Association between clinically abnormal observations and subsequent in-hospital mortality: a prospective study. *Resuscitation*. 2004;62(2):137-41. doi: 10.1016/j.resuscitation.2004.03.005. PubMed PMID: WOS:000223506500002.
20. Goldhill D, White S, Sumner A. Physiological values and procedures in the 24 h before ICU admission from the ward. *Anaesthesia*. 1999;54(6):529-34. doi: 10.1046/j.1365-2044.1999.00837.x. PubMed PMID: WOS:000081317400003.
21. Brown H, Terrence J, Vasquez P, Bates DW, Zimlichman E. Continuous Monitoring in an Inpatient Medical-Surgical Unit: A Controlled Clinical Trial. *The American Journal of Medicine*. 2014;127(3):226-32. doi: 10.1016/j.amjmed.2013.12.004.
22. Subbe C, Duller B, Bellomo R. Effect of an automated notification system for deteriorating ward patients on clinical outcomes. *Critical Care*. 2017;21(1). doi: 10.1186/s13054-017-1635-z.
23. Jones DA, DeVita MA, Bellomo R. Rapid-Response Teams. *NEJM*. 2011;365(2):139-46. doi: 10.1056/NEJMra0910926.
24. Brennan TA, Localio AR, Leape LL, et al. Identification of adverse events occurring during hospitalization. A cross-sectional study of litigation, quality assurance, and medical records at two teaching hospitals. *Annals of Internal Medicine*. 1990;112(3):221-6. doi: 10.7326/0003-4819-112-3-221.
25. Schimmel EM. The hazards of hospitalization. 1964. *Quality & safety in health care*. 2003;12(1):58-63; discussion -4.
26. Thomas EJ, Studdert DM, Burstin HR, et al. Incidence and Types of Adverse Events and Negligent Care in Utah and Colorado. *Medical Care*. 2000;38(3):261-71. doi: 10.1097/00005650-200003000-00003.
27. Wilson RM, Runciman WB, Gibberd RW, et al. The Quality in Australian Health Care Study. *The Medical journal of Australia*. 1995;163(9):458.
28. Davis P, Lay-Yee R, Briant R, Ali W, Scott A, Schug S. Adverse events in New Zealand public hospitals I: occurrence and impact. *N Z Med J*. 2002 ;115(1167):U271. PubMed PMID: 12552260.
29. McQuillan P, Pilkington S, Allan A, Taylor B, Short A, Morgan G, Nielsen M, Barrett D, Smith G. Confidential inquiry into quality of care before admission to intensive care. *BMJ*. 1998;316(7148):1853-8. doi: 10.1136/bmj.316.7148.1853.

30. Buist MD, Bernard SA, Waxman BP, Anderson J. Recognising clinical instability in hospital patients before cardiac arrest or unplanned admission to intensive care: A pilot study in a tertiary- care hospital. *Medical Journal of Australia.* 1999;171(1):22-5. doi: 10.5694/j.1326-5377.1999.tb123492.x.

31. Franklin C, Mathew J. Developing strategies to prevent inhospital cardiac arrest: analyzing responses of physicians and nurses in the hours before the event. *Critical Care Medicine*. 1994;22(2):244.

32. Hong W, Earnest A, Sultana P, Koh Z, Shahidah N, Ong MEH. How accurate are vital signs in predicting clinical outcomes in critically ill emergency department patients. European Journal of Emergency Medicine. 2013;20(1):27-32. doi: 10.1097/MEJ.0b013e32834fdcf3.

33. Philip KEJ, Pack E, Cambiano V, Rollmann H, Weil S, O'Beirne J. The accuracy of respiratory rate assessment by doctors in a London teaching hospital: a cross-sectional study. *Journal of Clinical Monitoring and Computing*. 2015;29(4):455.

34. Lovett PB, Buchwald JM, Stürmann K, Bijur P. The vexatious vital: Neither clinical measurements by nurses nor an electronic monitor provides accurate measurements of respiratory rate in triage. *Annals of Emergency Medicine*. 2005;45(1):68-76. doi: 10.1016/j.annemergmed.2004.06.016.

35. Yang S, Menne A, Hu P, Stansbury L, et al. Acoustic sensor versus electrocardiographically derived respiratory rate in unstable trauma patients. *J Clin Monit Comput*. 2017;31(4):765-72. Epub 2016/06/09. doi: 10.1007/s10877-016-9895-8. PubMed PMID: 27270963.

36. Kawanishi H, Inoue S, Kawaguchi M. A Retrospective Analysis of Oxygen Desaturation during Acoustic Respiratory Rate Monitoring in Non-ICU Patients following Tracheal Extubation after General Anesthesia. *Anesthesiol Res Pract*. 2017;2017:4203156. Epub 2017/05/11. doi: 10.1155/2017/4203156. PubMed PMID: 28487734; PMCID: PMC5405372.

37. Ouchi K, Fujiwara S, Sugiyama K. Acoustic method respiratory rate monitoring is useful in patients under intravenous anesthesia. *J Clin Monit Comput*. 2017;31(1):59-65. Epub 2016/01/14. doi: 10.1007/s10877-015-9822-4. PubMed PMID: 26759335.

38. McGrath SP, Pyke J, Taenzer AH. Assessment of continuous acoustic respiratory rate monitoring as an addition to a pulse oximetry-based patient surveillance system. *J Clin Monit Comput*. 2017;31(3):561-9. Epub 2016/05/05. doi: 10.1007/s10877-016-9884-y. PubMed PMID: 27142098.

39. Flenady T, Dwyer T, Applegarth J. Accurate respiratory rates count: So should you! *Australas Emerg Nurs J*. 2017;20(1):45-7. Epub 2017/01/12. doi: 10.1016/j.aenj.2016.12.003. PubMed PMID: 28073649.

40. Rodriguez-Molinero A, Narvaiza L, Ruiz J, Galvez-Barron C. Normal respiratory rate and peripheral blood oxygen saturation in the elderly population. *J Am Geriatr Soc*. 2013;61(12):2238-40. Epub 2013/12/18. doi: 10.1111/jgs.12580. PubMed PMID: 24329828.

41. Jungquist CR, Chandola V, Spulecki C, et al. Identifying Patients Experiencing Opioid-Induced Respiratory Depression During Recovery From Anesthesia: The Application of Electronic Monitoring Devices. *Worldviews Evid Based Nurs*. 2019;16(3):186-94. Epub 2019/05/02. doi: 10.1111/wvn.12362. PubMed PMID: 31050151.

42. Krieger J, Maglasiu N, Sforza E, Kurtz D. Breathing during sleep in normal middle-aged subjects. *Sleep*. 1990;13(2):143-54. Epub 1990/04/01. PubMed PMID: 2330473.

43. Ehsan Z, Mahmoud M, Shott SR, Amin RS, Isman SL. The effects of anesthesia and opioids on the upper airway: A systematic review. *Laryngoscope*. 2016;126(1):270-84. Epub 2015/07/23. doi: 10.1002/lary.25399. PubMed PMID: 26198715.

44. Drummond GB, Dhonneur G, Kirov K, Duvaldestin P. Effects of an opioid on respiratory movements and expiratory activity in humans during isoflurane anaesthesia. *Respir Physiol Neurobiol*. 2013;185(2):425-34. Epub 2012/09/05. doi: 10.1016/j.resp.2012.08.016. PubMed PMID: 22944354.

45. Al-Khabori M, Al-Riyami AZ, Al-Farsi K, et al. Validation of a non-invasive pulse CO-oximetry based hemoglobin estimation in normal blood donors. *Transfus Apher Sci*. 2014;50(1):95-8. Epub 2013/11/26. doi: 10.1016/j.transci.2013.10.007. PubMed PMID: 24268769.

46. Alakuijala A, Salmi T. Predicting Obstructive Sleep Apnea with Periodic Snoring Sound Recorded at Home. *J Clin Sleep Med.* 2016;12(7):953-8. Epub 2016/04/20. doi: 10.5664/jcsm.5922. PubMed PMID: 27092701; PMCID: PMC4918995.

47. Hong SN, Yoo J, Song IS, et al. Does Snoring Time Always Reflect the Severity of Obstructive Sleep Apnea? *Ann Otol Rhinol Laryngol*. 2017;126(10):693-6. Epub 2017/08/24. doi: 10.1177/0003489417727014. PubMed PMID: 28831834.

48. Koo SK, Kwon SB, Moon JS, Lee SH, Lee HB, Lee SJ. Comparison of snoring sounds between natural and drug-induced sleep recorded using a smartphone. *Auris Nasus Larynx*. 2017. Epub 2017/10/02. doi: 10.1016/j.anl.2017.09.005. PubMed PMID: 28964567.

49. Wu HT, Pan WY, Liu AB, et al. Vibration signals of snoring as a simple severity predictor for obstructive sleep apnea. *Clin Respir J*. 2016;10(4):440-8. Epub 2014/10/30. doi: 10.1111/crj.12237. PubMed PMID: 25354244.

50. Kulkas A, Huupponen E, Virkkala J, et al. Tracheal sound parameters of respiratory cycle phases show differences between flow-limited and normal breathing during sleep. *Physiol Meas.* 2010;31(3):427-38. Epub 2010/02/13. doi: 10.1088/0967-3334/31/3/010. PubMed PMID: 20150689.

51. Jungquist CR, Smith K, Nicely KL, Polomano RC. Monitoring Hospitalized Adult Patients for Opioid-Induced Sedation and Respiratory Depression. *The American Journal of Nursing*. 2017;117(3 Suppl 1):S27-S35. doi: 10.1097/01.NAJ.0000513528.79557.33. PubMed PMID: 28212147.

52. Holley K, MacNabb CM, Georgiadis P, et al. Monitoring minute ventilation versus respiratory rate to measure the adequacy of ventilation in patients undergoing upper endoscopic procedures. *J Clin Monit Comput*. 2016;30(1):33-9. Epub 2015/03/05. doi: 10.1007/s10877-015-9674-y. PubMed PMID: 25735263.

53. Ebert TJ, Middleton AH, Makhija N. Ventilation monitoring during moderate sedation in GI patients. *J Clin Monit Comput*. 2017;31(1):53-7. Epub 2015/12/03. doi: 10.1007/s10877-015-9809-1. PubMed PMID: 26628270.

54. Galvagno SM, Jr., Duke PG, Eversole DS, George EE. Evaluation of respiratory volume monitoring (RVM) to detect respiratory compromise in advance of pulse oximetry and help minimize false desaturation alarms. *J Trauma Acute Care Surg*. 2016;81(5 Suppl 2 Proceedings of the 2015 Military Health System Research Symposium):S162-S70. Epub 2016/10/22. doi: 10.1097/TA.0000000000001152. PubMed PMID: 27270857.

55. Voscopoulos C, Theos K, Tillmann Hein HA, George E. A risk stratification algorithm using non-invasive respiratory volume monitoring to improve safety when using post-operative opioids in the PACU. *J Clin Monit Comput*. 2017;31(2):417-26. Epub 2016/02/20. doi: 10.1007/s10877-016-9841-9. PubMed PMID: 26894592.

56. Voscopoulos CJ, MacNabb CM, Freeman J, Galvagno SM, Jr., Ladd D, George E. Continuous noninvasive respiratory volume monitoring for the identification of patients at risk for opioid-induced respiratory depression and obstructive breathing patterns. *J Trauma Acute Care Surg*. 2014;77(3 Suppl 2):S208-15. Epub 2014/08/28. doi: 10.1097/TA.0000000000000400. PubMed PMID: 25159358.

57. Mehta JH, Cattano D, Brayanov JB, George EE. Assessment of perioperative minute ventilation in obese versus non-obese patients with a non-invasive respiratory volume monitor. *BMC Anesthesiol*. 2017;17(1):61. Epub 2017/04/28. doi: 10.1186/s12871-017-0352-0. PubMed PMID: 28446134; PMCID: PMC5405482.

58. Kim KW, Choi HR, Bang SR, Lee JW. Comparison of end-tidal CO2 measured by transportable capnometer (EMMA capnograph) and arterial pCO2 in general anesthesia. *J Clin Monit Comput*. 2016;30(5):737-41. Epub 2015/08/13. doi: 10.1007/s10877-015-9748-x. PubMed PMID: 26264607.

59. Heines SJ, Strauch U, Roekaerts PM, Winkens B, Bergmans DC. Accuracy of end-tidal CO2 capnometers in post-cardiac surgery patients during controlled mechanical ventilation. *J Emerg Med*. 2013;45(1):130-5. Epub 2013/02/05. doi: 10.1016/j.jemermed.2012.11.019. PubMed PMID: 23375221.

60. Hutchison R. Capnography monitoring during opioid PCA administration. *J Opioid Manag*. 2006;2(4):207-8. Epub 2007/02/27. PubMed PMID: 17319481.

61. Oswald L, Zeuske T, Pfeffer J. Implementing Capnography in the PACU and Beyond. *J Perianesth Nurs*. 2016;31(5):392-6. Epub 2016/09/27. doi: 10.1016/j.jopan.2014.06.007. PubMed PMID: 27667345.

62. Lam T, Nagappa M, Wong J, Singh M, Wong D, Chung F. Continuous Pulse Oximetry and Capnography Monitoring for Postoperative Respiratory Depression and Adverse Events: A Systematic Review and Meta-analysis. *Anesth Analg*. 2017;125(6):2019-29. Epub 2017/10/25. doi: 10.1213/ANE.0000000000002557. PubMed PMID: 29064874.

63. Sivilotti ML, Messenger DW, van Vlymen J, Dungey PE, Murray HE. A comparative evaluation of capnometry versus pulse oximetry during procedural sedation and analgesia on room air. *CJEM*. 2010;12(5):397-404. Epub 2010/10/01. PubMed PMID: 20880431.

64. Carlisle H. Promoting the use of capnography in acute care settings: an evidence-based practice project. *J Perianesth Nurs*. 2015;30(3):201-8. Epub 2015/05/25. doi: 10.1016/j.jopan.2015.01.012. PubMed PMID: 26003766.

65. Langhan ML, Kurtz JC, Schaeffer P, Asnes AG, Riera A. Experiences with capnography in acute care settings: a mixed-methods analysis of clinical staff. *J Crit Care.* 2014;29(6):1035-40. Epub 2014/08/19. doi: 10.1016/j.jcrc.2014.06.021. PubMed PMID: 25129575; PMCID: PMC4194255.

66. Stites M, Surprise J, McNiel J, Northrop D, De Ruyter M. Continuous Capnography Reduces the Incidence of Opioid-Induced Respiratory Rescue by Hospital Rapid Resuscitation Team. *J Patient Saf*. 2017. Epub 2017/07/22. doi: 10.1097/PTS.0000000000000408. PubMed PMID: 28731933.

67. Ruiz Y, Farrero E, Córdoba A, González N, Dorca J, Prats E. Transcutaneous Carbon Dioxide Monitoring in Subjects With Acute Respiratory Failure and Severe Hypercapnia. *Respir Care*. 2016;61(4):428-33. Epub 2016/01/19. doi: 10.4187/respcare.04283. PubMed PMID: 26786741.

68. Horvath CM, Brutsche MH, Baty F, Rüdiger JJ. Transcutaneous versus blood carbon dioxide monitoring during acute noninvasive ventilation in the emergency department - a retrospective analysis. *Swiss Med Wkly*. 2016;146:w14373. Epub 2016/10/26. doi: 10.4414/smw.2016.14373. PubMed PMID: 27878795.

69. Conway A, Tipton E, Liu WH, et al. Accuracy and precision of transcutaneous carbon dioxide monitoring: a systematic review and meta-analysis. *Thorax*. 2019;74(2):157-63. Epub 2018/09/12. doi: 10.1136/thoraxjnl-2017-211466. PubMed PMID: 30209079.

70. Storre JH, Magnet FS, Dreher M, Windisch W. Transcutaneous monitoring as a replacement for arterial PCO(2) monitoring during nocturnal non-invasive ventilation. *Respir Med*. 2011;105(1):143-50. Epub 2010/10/28. doi: 10.1016/j.rmed.2010.10.007. PubMed PMID: 21030230.

71. Medicare Cf, Services M. Requirements for hospital medication administration, particularly intravenous (IV) medications and post-operative care of patients receiving IV opioids. 2017.

72. Berry RB, Brooks R, Gamaldo C, et al. AASM Scoring Manual Updates for 2017 (Version 2.4). *J Clin Sleep Med*. 2017;13(5):665-6. Epub 2017/05/15. doi: 10.5664/jcsm.6576. PubMed PMID: 28416048; PMCID: PMC5406946.

73. Voepel-Lewis T, Parker ML, Burke CN, et al. Pulse oximetry desaturation alarms on a general postoperative adult unit: a prospective observational study of nurse response time. *International Journal of Nursing Studies*. 2013;50(10):1351-8. doi: 10.1016/j.ijnurstu.2013.02.006. PubMed PMID: 23474081.

74. American Society of Anesthesiologists Task Force on Neuraxial O, Horlocker TT, Burton AW, Connis RT, et al. Practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration. *Anesthesiology*. 2009;110(2):218-30. Epub 2009/02/06. doi: 10.1097/ALN.0b013e31818ec946. PubMed PMID: 19194148.

75. Miner JR, Moore JC, Plummer D, Gray RO, Patel S, Ho JD. Randomized clinical trial of the effect of supplemental opioids in procedural sedation with propofol on serum catecholamines. *Acad Emerg Med*. 2013;20(4):330-7. Epub 2013/05/25. doi: 10.1111/acem.12110. PubMed PMID: 23701339.

76. Chung F, Liao P, Elsaid H, Islam S, Shapiro CM, Sun Y. Oxygen desaturation index from nocturnal oximetry: a sensitive and specific tool to detect sleep-disordered breathing in surgical patients. *Anesth Analg*. 2012;114(5):993-1000. Epub 2012/03/01. doi: 10.1213/ANE.0b013e318248f4f5. PubMed PMID: 22366847.

77. Pedersen T, Nicholson A, Hovhannisyan K, et al. Pulse oximetry for perioperative monitoring. Cochrane Database Syst Rev. 2014(3):CD002013. Epub 2014/03/19. doi: 10.1002/14651858.CD002013.pub3. PubMed PMID: 24638894.

78. Guide H-t. Prevent Harm From High-Alert Medications. Cambridge, MA: Institute for Healthcare Improvement. 2012.

79. Taenzer AH, Pyke JB, McGrath SP, Blike GT. Impact of pulse oximetry surveillance on rescue events and intensive care unit transfers: a before-and-after concurrence study. *Anesthesiology*. 2010;112(2):282-7. Epub 2010/01/26. doi: 10.1097/ALN.0b013e3181ca7a9b. PubMed PMID: 20098128.

80. Rozario L, Sloper D, Sheridan MJ. Supplemental oxygen during moderate sedation and the occurrence of clinically significant desaturation during endoscopic procedures. *Gastroenterol Nurs*. 2008;31(4):281-5. Epub 2008/08/19. doi: 10.1097/01.SGA.0000334034.94370.bf. PubMed PMID: 18708832.

81. Fu ES, Downs JB, Schweiger JW, Miguel RV, Smith RA. Supplemental oxygen impairs detection of hypoventilation by pulse oximetry. *Chest*. 2004;126(5):1552-8. doi: 10.1378/chest.126.5.1552. PubMed PMID: 15539726.

82. Maddox RR, Williams CK, Oglesby H, Butler B, Colclasure B. Clinical

experience with patient-controlled analgesia using continuous respiratory monitoring and a smart infusion system. *Am J Health Syst Pharm*. 2006;63(2):157-64. Epub 2006/01/05. doi: 10.2146/ajhp050194. PubMed PMID: 16390930.

83. Sun Z, Sessler DI, Dalton JE, Devereaux PJ, et al. Postoperative Hypoxemia Is Common and Persistent: A Prospective Blinded Observational Study. *Anesth Analg*. 2015;121(3):709-15. Epub 2015/08/20. doi: 10.1213/ANE.0000000000000836. PubMed PMID: 26287299; PMCID: PMC4825673.

84. Weiniger CF, Carvalho B, Stocki D, Einav S. Analysis of Physiological Respiratory Variable Alarm Alerts Among Laboring Women Receiving Remifentanil. *Anesth Analg.* 2017;124(4):1211-8. doi: 10.1213/ANE.0000000000001644. PubMed PMID: 27870644.

85. Chung F, Liao P, Yang Y, et al. Postoperative sleep-disordered breathing in patients without preoperative sleep apnea. *Anesth Analg*. 2015;120(6):1214-24. doi: 10.1213/ANE.0000000000000774. PubMed PMID: 25988633.

86. Vincent JJ-L, Einav KS, Pearse KR, et al. Improving detection of patient deterioration in the general hospital ward environment. *European Journal of Anaesthesiology*. 2018;35(5):325-33. doi: 10.1097/EJA.0000000000000798.

87. Oderda, G.M., Gan, T.J., Johnson, B.H., Robinson, S.B. Effect of Opioid-Related Adverse Events on Outcomes in Selected Surgical Patients. *Journal of Pain & Palliative Care Pharmacology*. 2013; 27:62-70

88. Culler, S.D., McGuire, K.J., Little, K.M., Jevsevar, D., Shea, K., Schlosser, M., Ambrose, K.E., Simon, A.W. Incremental Hospital Cost and Length –of-stay Associated with Treating Adverse Events Among Medicare Beneficiaries Undergoing Cervical Spinal Fusion During Fiscal Year 2013 an 2014. *Spine*. 2017; 42 (20) 1578-1586.

89. Culler SD; Jevsevar DS; Shea KG; Wright KK; Simon AW. The Incremental hospital cost and length of stay associated with treating adverse events among Medicare benificiaries undergoing TKA. *Journal of Arthroplasty*. 2015 30(1):19-25.

90. Portuondo JI, Shah SS, Singh H, Massarweh NN. Failure to Rescue as a Surgical Quality Indicator; current concepts and future directions for improving surgical outcomes. *Anesthesiology*. 2019;131(2):426-437. doi: 10.1097/ALN.0000000000002602.

91. Chalfin D. Cost-effectiveness analysis in health care. *Hospital cost management and accounting*. 1995;7(4):1.

92. Slight PS, Franz VC, Olugbile WM, Brown WH, Bates WD, Zimlichman WE. The Return on Investment of Implementing a Continuous Monitoring System in General Medical-Surgical Units*. *Critical Care Medicine*. 2014;42(8):1862-8. doi: 10.1097/CCM.0000000000000340.

93. Halpern AN, Pastores MS, Oropello MJ, Kvetan MV. Critical Care Medicine in the United States: Addressing the Intensivist Shortage and Image of the Specialty.* *Critical Care Medicine*. 2013;41(12):2754-61. doi: 10.1097/CCM.0b013e318298a6fb.

94. Gooch R, Kahn J. ICU Bed Supply, Utilization, and Health Care Spending An Example of Demand Elasticity. *JAMA*2014;311(6):567-8. doi: 10.1001/jama.2013.283800. PubMed PMID: WOS:000330941000007.

95. McGrath SP, Perreard IM, Garland MD, Converse KA, Mackenzie TA. Improving Patient Safety and Clinician Workflow in the General Care Setting With Enhanced Surveillance Monitoring. IEEE *Journal of Biomedical and Health Informatics*. 2019;23(2):857-66. doi: 10.1109/JBHI.2018.2834863.

96. Taaenzer A, Bilke G. Patient acceptance and cost-effectiveness are key factors in postoperative monitoring. *APSF*. 2012;27(1):121.

97. Abenstein JP, Narr BJ. An ounce of prevention may equate to a pound of cure: Can early detection and intervention prevent adverse events? *Anesthesiology*. 2010;112(2):272-273. doi:10.1097/ALN.0b013e3181ca858d