Postoperative Cesarean Section Outcomes Following Standardized Oxytocin Dosing: Rule of Three's

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A DNP Project Manuscript
Submitted in Partial Fulfillment of the Requirements for the
Doctor of Nursing Practice Degree

University of Maryland School of Nursing
May 2020

Abstract

Problem & Purpose: Currently there is no standardized guidelines for the administration of oxytocin during a cesarean section to prevent uterine atony, which has led to anesthesia providers administering varying doses of oxytocin to prevent postpartum hemorrhage (PPH). Oxytocin that is delivered at high rates of infusion have been associated with myocardial depression through hypotension, tachycardia, and myocardial ischemia. The literature has shown that the use of regimental low dosed oxytocin like the "Rule of Three's" improves its efficacy. The purpose of this quality improvement (QI) project is to overcome the lack of standardization with the delivery of oxytocin during a cesarean section by developing a clinical practice guideline (CPG) for low dose oxytocin administration following the "Rule of Three's" algorithm. This manuscript will highlight the development with a primary concentration on the post-cesarean section oxytocin administration.

Methods: The CPG was developed through 4 phases. The first phase involved stakeholder recruitment along with the development of the CPG using the AGREE II tool to evaluate it. During the second phase the CPG was appraised by the chief anesthesiologist for initial approval. The third phase consisted of a formal presentation to the anesthesia staff that was based on oxytocin management. A Provider Feedback Questionnaire (PFQ) was used to evaluate providers response to CPG. During the fourth stage, approval for the use the CPG was granted by the chief anesthesiologist for use. The data was analyze confidentially using both inferential and descriptive statistics.

Results: The CPG was assessed using the AGREE II Tool resulting in an overall average of 93%, which was indicative of a high-quality guideline recommended for clinical use at the facility. The PFQ (n=12) assessed the CPG's quality, acceptance, applicability, value, and outcome had an overall agreement of 80.7%.

Conclusion: The "Rule of Three's" was proven to be the optimal dosing regimen during cesarean section and throughout the postoperative period. During the postoperative period the prevention of uterine atony is vital to reduce the incidence and severity of PPH, which is effectively achieved when using the "Rule of Three's" CPG. A limitation of the quality improvement (QI) project was anesthesia provider were resistant to changing their practice. The next phase of the QI project will include reducing provider resistance and monitoring quantitative blood loss during surgery.

Introduction

During a cesarean section there are many risk and complications that may arise, the prudent anesthesia provider needs to be vigilant to monitor blood loss and understand the risk associated with PPH and how to prevent it. According the World Health Organization postpartum hemorrhage is responsible for approximately 25% of maternal deaths worldwide (World Health Organization [WHO], 2017). The Centers for Disease Control and Prevention published data has shown an increasing trend in the severity of postpartum hemorrhage that has led to more patients requiring the need for blood product during delivery, with a rate of transfusion of 7.9 per 10,000 in 1993 that has increased to 39.7 per 10,000 in 2014 (Centers for Disease Control and Prevention [CDC], 2015).To help reduce the incidence of postpartum hemorrhage it is common practice to administer a uterotonic agent such as oxytocin.

Currently there is no standardized policy for the administration of oxytocin nationally or within the organization of interest. Oxytocin is most often supplied as 30 international units (IU) in 500 mL of normal saline and routinely infused as a bolus for the duration of the procedure following delivery of the placenta. This often results in the anesthesia provider administering a large quantity of oxytocin over a very short period of time; that can often exceed 30 IU administered in as little as 10-30 minutes that leads to hypotension, tachycardia, and myocardial ischemia (Kovacheva, Soens, & Tsen, 2015). The continuation of a low-dose oxytocin infusion during the postoperative period is vital to reduce the incidence of oxytocin sensitization that can lead to PPH during this recovery phase (Yamagucih, Siaulys, & Torres, 2016). The purpose of this project was to standardize the delivery of oxytocin using the optimal dosing regimen "Rule

of Three's" to ensure the controlled delivery to the parturient during a cesarean section and throughout the postoperative period to improve its efficacy.

Literature Review

A literature review was performed examining the best evidence-based practice to help develop the CPG (Table 1). The literature review examined studies that were performed within the last ten years and included 7 randomize control trial (RCT), a single-blinded dual-arm dose response study, and a retrospective study. The literature review revealed a common premise regarding oxytocin administration. This included the use of smaller oxytocin bolus doses initially followed by a low dose oxytocin infusion improved the efficacy of oxytocin when compared to a rapid high dose infusion. The literature was consistent in recommending the adoption of low dose oxytocin bolus followed by an infusion to prevent PPH and hemodynamic depression while preserving uterine tonicity (UT) during a cesarean section.

The use of lower doses of oxytocin given by bolus and infusion during a cesarean section was noted to have beneficial outcomes for maintaining UT while reducing hemodynamic depression. Duffield and associates performed an RCT that examined the effects of a low dose infusion (2.5 U/h) versus a high rate infusion (15 U/h). They determined that the use of low dose infusion provided adequate UT in a timely manner with an estimated blood loss that was comparable to higher infusions rates, while producing less hypotension, tachycardia, and myocardial depression seen with higher infusions (Duffield et. al., 2017). The implementation of a standardized oxytocin administration protocol has been associated with reducing the overall requirements of oxytocin while preserving UT throughout the postoperative period. Kovacheva and associates examined 60 patients in an RCT that identified the effects of a "Rule of Three's" algorithm on preventing postpartum hemorrhage and the adverse effects of oxytocin. This study

examined the effect of 3 units of oxytocin bolus with determined three-minute intervals for monitoring UT and discovered that following the "Rule of Three's" algorithm resulted in adequate UT within 3 minutes with no parturient exhibiting uterine atony after 9 minutes (Kovacheva, Soens, & Tsen, 2015).

The use of a higher dosed oxytocin bolus and infusion can lead to increased uterine atony and PPH due to oxytocin receptor sensitization during the postoperative period (Yamagucih, Siaulys, & Torres, 2016). The use of the "Rule of Three's" reduces the risk of oxytocin desensitization and improves its efficacy by allowing for a controlled administration during the intraoperative period throughout the postoperative period (Kovacheva, Soens, & Tsen, 2015; Yamagucih, Siaulys, & Torres, 2016). The American College of Obstetricians and Gynecologist practice bulletin currently suggest that 10 U diluted oxytocin bolus should be administered to prevent uterine atony (American College of Obstetricians and Gynecologist [ACOG], 2017). Bansal and colleagues performed an RCT with 271 participants and uncovered that 10 U of oxytocin over 2-4 hours provided just as adequate uterine tone with no increase in hemorrhage or transfusion compared to 30 U oxytocin over 8-12 hour, while providing better prevention of atony and less fluctuations in vital signs (Bansal, Cecilia, Vijayaselvi, Lakshmi, & Jose, 2018). Ghulmiyyah and associates performed an RCT with 189 patients in three different groups (n = 63) who received varying total doses of oxytocin (20, 30, and 40 units) throughout the perioperative period. This study concluded that 20 U of oxytocin provided comparable reduction in PPH with no postoperative decrease in systolic or diastolic blood pressure (Ghulmiyyah et. al., 2016). The literature review suggested that the continuation of low dose oxytocin should be continued throughout the postoperative period. During this period, it is crucial that oxytocin administration is limited to the lower suggested dosages of a total of 10 U and should not exceed

4 hours of delivery time to reduce the incidence of hemodynamic depression that leads to myocardial depression.

Theoretical Framework

Lewin's Theory of Change (LTC) is a middle-range theory that was used to provide the theoretical framework to address the issue of changing the oxytocin protocol within the organization by identifying driving forces, restraining forces, and initiating equilibrium (Lewin, 1947). The purpose of LTC is to help organizations improve patient outcomes by identify a needed change; then implementing the best practice to achieve the desired state while navigating resistance (Husaain et. al., 2018). The key concept of LTC is to "unfreeze" habits of staff, then implementing the change followed by "refreezing" the new change to become a habit amongst staff (Hussaain et. al., 2018).

The LTC was deployed to help instill the oxytocin "Rule of Three's" CPG for cesarean section within the organization. During the first stage (unfreezing), high level evidence-based findings were delivered to the providers regarding standardized oxytocin administration that offered information on why a practice change was needed . Stakeholder and champions were identified to help garner buy in within the department to help overcome denial and doubt that the staff might have. During the implementation phase a new CPG was initiated, during this period it was important to frequently follow-up and assess the providers knowledge on the practice change instituted. Lewin's mentioned that during the transitional period it is vital to understand that the desired change may meet resistance due to the learning curve and this phase will take time to navigate resistance from staff (Lewin, 1947). The final phase of the LTC is the "refreezing", where the intended change will become the new norm or habit for the anesthesia providers within the organization. During this stage the "rule of three's" CPG was instituted

within the organization. To ensure the successful integration of the "rule of three's" CPG into the organizations practice it was important to continue monitoring the changes made and make adjustments to ensure its success.

Methods

During this QI project a low-dose oxytocin CPG was developed for use by anesthesia providers within an inner-city community hospital in Baltimore, MD that provided obstetrical services for more than 5000 patients yearly (refer to Appendix A). The CPG was developed with three main foci that included hemodynamic maintenance, intraoperative management and postoperative management. This project focused on patients who underwent an elective or non-elective cesarean section, while excluding patients who endured an emergent cesarean section.

The CPG was developed and implemented over four phases. During the first phase a literature review was performed to examine the best practice available for the administration of oxytocin during a cesarean section. Stakeholders and champions were identified within the organization and were recruited to join the oxytocin taskforce. The members of the team included three Doctoral of Nursing Practice (DNP) nurse anesthetist students and two nurse anesthetists. A CPG was developed by the DNP students and disseminated to the nurse anesthetist stakeholders for evaluation using the Appraisal of Guidelines for Research and Evaluation (AGREE II) tool. Changes to the CPG were then made based on the results from the AGREE II tool. During the second phase the CPG was presented to the chief anesthesiologist for appraisal and approval for use within the department. The third phase then consisted of a formal presentation by the DNP students on oxytocin management using the best current literature for the "Rule of Three's" CPG to the anesthesia department during a weekly meeting. At the conclusion of the meeting a Provider Feedback Questionnaire (PFQ) was disseminated to the

anesthesia providers to fill out anonymously. The PFQ was then reviewed by the team and adjustments to the CPG were made accordingly, based on the results. The finial CPG was then granted approval for use within the organization by the chief anesthesiologist.

To assess the quality of the "Rule of Three's" CPG the AGREE II tool was used to assess transparency and rigor of the CPG within the organization. The AGREE II was disseminated to the stakeholders who were all nurse anesthetist, the chief CRNA, and the chief MDA. The AGREE II tool consist of 23 items within 6 domains: *Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability,* and *Editorial Independence* (AGREE Next Steps Consortium, 2013). Each aspect of the CPG is assessed through the 23 items and scored by each appraiser using a 7-point Likert Scale to identify any limitations while recognizing strengths of the CPG. A Provider Feedback Questionnaire (PFQ) was used and allowed anesthesia providers to assess the oxytocin CPG. The AGREE II results were collected for each of the 23 items and each response was then calculated and assigned a domain score that was designated as a percentage . To assess reliability and validity of the AGREE II tool a Cronbach alpha coefficient score was performed with a score of 0.88 which is suggestive of high validity.

The PFQ provides 23 questions on a 3-point Likert Scale with the following options: strongly agree, neither agree or disagree, and strongly disagree that assesses the confidence of provider adoption (Brouwers et. al., 2004). Anesthesia providers were also asked to provide demographic information regarding educational background and years of experience within the PFQ (refer to Appendix B). They were then asked to evaluate the usability of the CPG using the PFQ. The PFQ responses were tallied and a percentage based out of total responses for each

question was assigned to each section. These findings were then shared with the stakeholders and the CPG was tailored to fit the clinical practice of the organization.

Results

During this QI project the team confronted the structure and processes of oxytocin administration within the institution which consisted of high dosages and rapid infusion. The goal of this project was to improve knowledge amongst anesthesia providers regarding perioperative oxytocin use throughout the postoperative period. The change that was introduced incorporated the use of standardized oxytocin regimen known as the "Rule of Three's". This incorporated a small oxytocin bolus dose of 3 IU followed by a low dose infusion of 2.5 U/h that does not exceed a total of 10 U or an infusion time of 4 hours throughout the postoperative period (Bansal, Cecilia, Vijayaselvi, Lakshmi, & Jose, 2018; Duffield et. al., 2017; Kovacheva, Soens, & Tsen, 2015). The goal of the project was that anesthesia providers would adopt the use of the oxytocin CPG within their practice. The development of the CPG used current evidence-based oxytocin management literature and an intraoperative oxytocin administration algorithm was created to help standardize the delivery of oxytocin during the cesarean delivery (Figure 1).

To assess the quality of the CPG during the first phase of development the AGREE II tool results were calculated and evaluated following the guidelines set forth for each domain (Table 2). The overall calculated results for each domain score were as follows: *Scope and Purpose* (90%), *Stakeholder Involvement* (89%), *Rigors of Development* (90%), *Clarity of Presentation* (94%), *Applicability* (97%), *Editorial Independence* (97%) with an overall score of (93%). The results of the AGREE II tool revealed that the CPG that was developed was of high quality. Following review of the results with stakeholders, adjustments to the CPG were then initiated to ensure its adoption into practice.

The oxytocin CPG was presented to the anesthesia staff and PFQ's were obtained to gather demographic information and evaluate the providers opinion on the oxytocin low dose CPG (Table 3). The PFQ's were completed anonymously and securely stored within in a lock box. The response rate for the PFQ's was 86% (Figure 2). The demographics looked at credentials of nurse anesthetist (n=8) and anesthesiologist (n=4); along with years of experience with an average of 12.7 years for the nurse anesthetist and 14.3 years for the anesthesiologist (Figure 3). The percentages of agreement for the domains of the PFQ were as follows: *Quality* (96%), *Acceptance of Recommendations* (76%), *Applicability of Recommendations* (27%), *Comparative Value* (88%), and *Outcome Variables* (86%). The PFQ's overall agreement score was 80.7% for the CPG.

During the development of this project there were many facilitators and barriers identified throughout each phase. The main facilitator for the use of the "Rule of Three's CPG was the improved patient outcomes noted within the evidence-based literature. There was a consistent theme noted of improved oxytocin efficacy with low controlled dosage through the mitigation of hemodynamic instability that improved rates of myocardial depression seen with higher oxytocin doses. Barriers to implementation that were identified included resistance from anesthesia provider to change their oxytocin administration practice and the complexity of infusion pumps setup. The programing of complex infusion pumps requires additional training of staff to reduce the risk of administration errors. Providers were manually calculating the dosage and entering the value into the infusion pump.

Discussion

The results of the AGREE II tool demonstrated a high-quality CPG with a high overall assessment score (93%), which was indicative of likely adoption within the organization.

The results of the PFQ revealed that most of the anesthesia providers accepted that the CPG should be approved for practice (75%). Although, the CPG and the PFQ both scored favorably amongst providers within the organization there was an observed resistance to the practice change within the department. Findings within the PFQ revealed that a provider predisposition for oxytocin use still needed to be overcome to facilitate the incorporation of the evidence-based practice changes. Overall, the results of the AGREE II tool and PFQ demonstrated that the "Rule of Three's" CPG was likely to be successfully adopted into practice within the organization, while ensuring the standardization of oxytocin administration during cesarean deliveries.

Strengths of the "Rule of Three's" CPG development included an easy to follow algorithm that helps guide anesthesia providers through the administration of the bolus, infusion dosing, setup, and follow up communication with obstetrician during a cesarean section. The institution of the CPG will improve oxytocin efficacy by reducing the hemodynamic depression associated with rapid high dose administration of oxytocin. The literature review revealed that the "Rule of Three's" had consistently shown improvements of patient outcomes while reducing adverse events, because of this it was selected to guide the development of the CPG. The evaluation of the CPG was performed by anesthesia providers using both the AGREE II and PFQ which are both reliable CPG assessment tools. Weakness identified within the CPG project was the specificity of the study. The CPG only examined elective cesarean delivers and did not evaluate emergent deliveries or the parturient who were exposed to an oxytocin infusion prior to a cesarean delivery.

Limitation noted during this projected included bias, which effected the internal validity; the study was based on oxytocin administration for the parturient who underwent a scheduled cesarean section, while recusing emergent cesarean deliveries. Approximately half of the

anesthesia providers within the department completed the PFQ, which lead to a smaller sample size than desired for feedback. During this project qualitative observation and datum was used to guide the development of the CPG, while quantitative datum was not collected during this time.

Conclusion

The development and institution of the "Rule of Three's" CPG has allowed for the standardized delivery of oxytocin during cesarean section within the organization. This has afforded anesthesia providers the ability to administer oxytocin in a controlled manner. Evidence suggest that the standardized delivery of oxytocin using the "Rule of Three's" would decrease the risk of cardiac depression during a cesarean section, while providing adequate uterine tonicity to prevent postpartum hemorrhage (Duffield et. al., 2017; Kovacheva, Soens, & Tsen, 2015). Thus, improving the overall efficacy of oxytocin administration and management during a cesarean delivery.

To ensure sustainability within the department and among anesthesia providers it is vital to continue quarterly evaluations of compliance with the "Rule of Three's" CPG. The anesthesia staff should also be provided yearly continuing education on the CPG to help overcome bias within their practice. To continue the progression of the CPG it is essential to also educate obstetricians, pharmacist, and labor and delivery nurses on the most current evidence to ensure continuation of the low dose oxytocin throughout the postoperative period. This will also help garner buy in and recruit new stakeholders, which will ultimately lead to the development of a multidisciplinary team that will lead future endeavors for the advancement of the CPG. Future recommendation of research that will help continue the development of the oxytocin CPG includes a study that will examine quantitative blood loss during a cesarean section using the "Rule of Three's" compared to the older rapid high dose oxytocin administration. This incidence

of hemodynamic change should also be assessed by examining phenylephrine and ephedrine dosage requirements during each oxytocin delivery strategy. Finally, the incidence of uterine atony requiring secondary uterotonic agents (carboprost and methergine) when using the "Rule of Three's" CPG should be examined.

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Table 1. *Evidence Review Table*

Author, year	Study objective/ intervention or exposures compared	Design	Sample (N)	Outcomes studied (how measured)	Results	*Level and Quality Rating
Lavoie, McCarthy, & Wong, 2015	Identify the effective dose of oxytocin in 90% of parturient to increase uterine tone while decreasing the incidence of hemodynamic changes and hemorrhage.	Single-blinded, dual-arm, dose-response study using a 9:1 biased-coin sequential allocation method.	N=70 Nonlaboring group n=38 Laboring group n=32	1) Outcomes measured was the ED90 for satisfactory uterine tone deemed the obstetrician following administration. 2) Estimated ED90 was calculated through equation using the delta method.	1) Parturient who were exposed to oxytocin during labor required an approximately 3 times greater dose compared to the nonlaboring patient who had an elective cesarean section. 2) Patients who received 10 IU of oxytocin or greater had increased incidence of hypotension, tachycardia, myocardial ischemia, and arrhythmias. 3) The ED90 in the nonlaboring patient was determined to be 0.35 IU. The ED90 of the laboring parturient is 2.99 IU.	III A
Kovacheva, Soens, & Tsen, 2016	1) Determine if the use of the "Rule of Threes" algorithm (3IU oxytocin, timed uterine tone evaluations, and a systematic use of alternative uterotonic agents) will reduce the dose requirements of oxytocin to achieve adequate uterine tone following cesarean section. 2) The "Rule of Threes" group	Double-blinded, Randomized Control Trial	N=60 Rule of threes algorithm n=30 Continuous infusion oxytocin n=30	1) Outcomes measures was the total amount of oxytocin and time needed to achieve adequate uterine tone. 2) Uterine tone was assessed manually and rated on a linear analog scale (0-10) by the obstetrician at the 3,6,9, and 12-minute mark.	1) Lower oxytocin doses where required to achieve adequate uterine tone (4.0 vs. 8.4 IU). 2) Additional uterotonic agents were not required with the rule of threes algorithm. 3) No difference noted in maternal hemodynamics, uterine tone, hemorrhage, and side effects.	II A

	received 3 IU of oxytocin IV push followed by a wide-open infusion of 0.9% normal saline. The standard care group received a 3 ml IV push of 0.9% normal saline followed by a wide-open infusion of oxytocin (30 IU in 0.9% normal saline)					
Butwick, Coleman, Chen, Riley, & Carvalho, 2010	To Determine the lowest effective bolus dose of oxytocin that will produce adequate uterine tone at 2 minutes for 50% and 95% of patients receiving an elective Cesarean deliver with spinal anesthesia.	Double-blinded, Randomized Control Trial	N=75 0 U oxytocin n=15 0.5 U oxytocin n=15 1 U oxytocin n=15 3 U oxytocin n=15 5 U oxytocin n=15	Two subjective assessments of uterine tone used following uterine message by the obstetrician: adequate or inadequate uterine tone, and a uterine tone scale using a verbal numeric scale of 0-10 (0, no uterine tone; 10, optimal uterine tone)	1) Patients who received the 3U and 5U dose of oxytocin had higher verbal numeric scores and as well as a higher percentage of adequate uterine tone at 2,3,6,and 9 minutes (3U; 100%: 5U; 93-100%) compared to the lower doses of oxytocin. 2) Less blood loss was noted with the 3U and 5U groups with an EBL of 707 ml and 697 ml respectively, compared to the placebo group which had an average of 800 ml of EBL. 3) Hypotension (10% decrease in MAP) occurred at a higher rate with the 5U group, while the 3U group had an equivalent rate of hypotension as the 0.5U group.	II A
Duffield, et. al., 2017	To determine how the rate of infusion of oxytocin effects uterine tone and influences total	Double-blinded, Randomized Control Trial	N=51 women undergoing elective cesarean section under neuraxial anesthesia	1) EBL was measured quantitatively by a blinded study investigator who was not involved with the care of the patient at	1) The difference in EBL between the two infusion rates was 22 mL with a 95% confidence interval (-158 to 236).	II A

	blood loss during cesarean delivery. . Both groups received a 1 unit oxytocin bolus; while then either beginning a 2.5 U/h or 15 U/h maintenance infusion of oxytocin.		2.5 U/h n=24 15 U/h n=27	the end of surgery. EBL was calculated using the following values: EBL in canister, EBL around surgical field, and electronical weight measurement of all blood-soaked laps. 2) The uterine tone was assessed subjectively by asking the obstetrician if uterine tone was adequate at two-minute intervals within the first two minutes who would reply with a "yes" or "no". 3) An anesthesia record review assessed the use of uterotonics, rescue doses or any hemodynamic changes during the procedure.	2) There was no significant difference in the rate of postpartum hemorrhage between the two groups. 3) There was no time interval difference between the two groups to achieve adequate uterine tone. 4) The use of low dose infusion provides adequate uterine tone in a timely manner with and estimated blood loss that is comparable to higher infusions rates, while producing less hemodynamic changes of hypotension and tachycardia seen with higher infusions.	
Sheehan et. al., 2011	Compared the use of 5 IU oxytocin bolus followed by an oxytocin infusion (40 IU in 500 mL of saline infused over 4 hours)vs placebo infusion of saline (500	Large multicenter double-blind, randomized control trial	N= 2069 women receiving elective cesarean section. Bolus only n=1025 Bolus and infusion n=1033	1) Quantitative calculation of preoperative and postoperative packed cell volume and estimated hemorrhage during cesarean section by measuring swab weight and disposable waterproof drapes with pockets to	1) There was no significant difference in the amount of hemorrhage between the two groups. The occurrence of post-operative anemia was high between the two groups, but no statistical significance. 2) the oxytocin infusion group had higher incidence of adequate uterine tone, thus had lower requirement for additional uterotonic agent administration during the trial.	II B

	mL over 4 hours) to determine if there was a reduction in obstetric hemorrhage and use of uterotonic agents.			measure. They also monitored hemoglobin for 20% drop within 48 hours and monitored for side effects such as nausea, vomiting, and hypotension. 2) Observed and recorded use of uterotonic agents during the procedure since it is used to treat uterine atony and increase uterine tone to reduce bleeding in the parturient.		
DaGraca, Malladi, Nunes, & Scavone, 2013	Determine if the implementation of low dose oxytocin infusion policy provided adequate uterine tone without an increase in postpartum hemorrhage. Compared charts 6 months prior and 6 after the institution of oxytocin protocol.	Retrospective review	N=1572 Pre-protocol n=800 Post-protocol n=772	1) To monitor postpartum hemorrhage researches reviewed the patients pre and post hemoglobin levels and noted the PRE-group median difference was 1.6 g/dL, while the POST groups median hemoglobin was a 1.1 g/dL difference. 2) they also reviewed the operative records to see the use of secondary uterotonic agents for the treatment of uterine atony.	) Primary outcome of study found that postpartum hemorrhage in the group six months prior to intervention occurred in 15.1% of the patients who had cesarean delivery. The post intervention group had a 12.5% occurrence of postpartum hemorrhage following cesarean delivery. 2) Secondary outcome of the study found a 99.4% compliance rate with the adoption of the postpartum oxytocin infusion protocol that that was instituted	III A

Tae-Sung, Jun-Seok, Jung-Man, & Sin-Kyu, 2011	Examined the hemodynamic, EBL, and uterine tone effects oxytocin has when delivered by a continuous infusion (0.5 IU/min) versus a bolus followed by lower infusion rate (2 or 5 IU bolus then 0.25 IU/min infusion) in cesarean delivery with spinal anesthesia.	Randomized control trial	N=60 Infusion group n=20 2 IU followed by infusion n=20 5 IU followed by infusion n=20	1) Uterine tone was assessed subjectively using through palpitation on a linear analog scale at set intervals of 5, 10, 15, 20, and 25 minutes. 2) Changes in hemodynamics were assessed by assessing MAP and HR prior to delivery of oxytocin compared to time of maximum change.	1) Uterine tone significantly increased with the use of bolus followed by the infusion. The infusion only group had 30% incidence of additional uterotonic agent use. 2) All of the studies group had adequate uterine tone by 10 minutes. 3) Higher initial bolus dose of 5 IU was associated with higher incidence of hypotension compared to the 2 IU, and no bolus infusion groups.	II A
Cecilia, Vijayaseivi, Bansai, Lakshmi, & Jose, 2018	Examined the efficacy of 10 U oxytocin compared to 30 U in preventing postpartum hemorrhage, or deterioration in vital signs as well as need for blood transfusion	Randomized control trial, double-blinded	N= 271 10 U oxytocin group n=135 30 U oxytocin group n=136	1) The need for additional uterotonic agent was assessed as well as a change in hemodynamic stability by monitoring for changes in HR or BP. 2) A significant decline in preoperative and postoperative packed cell volume was assessed, with a difference of greater than 10% being deemed significant.	1) Low dose oxytocin of 10 units over 2-4 hours was just as effective as higher dose oxytocin 30 U over 8-12 hours to preventive postpartum hemorrhage. 2) There were no statistically significant differences in hemorrhage, need for additional uterotonic or blood transfusion. 3) Lower dose oxytocin did have less vital sign fluctuations and instability as well as less incidence of uterine atony.	II A
Ghulmiyyah, Usta, Taher, Abu-Ghannam, Tamim, & Nassar, 2016	Examined optimal dose of oxytocin during elective cesarean section throughout the	Randomized control trial, double-blinded	N= 189 20 U group n = 63 30 U group n = 63	1) hemoglobin pre and post levels were examined to assess PPH as well as calculated total blood loss. There was not a	1) 20 U oxytocin was determined to be the optimal oxytocin dose for elective cesarean section.	II A

	postoperative period. The study reviewed total dosages of 20 U, 30 U, and 40 U of oxytocin and the clinical effects it had on PPH compared to adverse effects at each respective dose.		40 U group n = 63	significant difference in the volume for blood loss between the different groups 2) The incidence of intraoperative and postoperative hemodynamic changes was assessed. There was no significant change in postoperative systolic or diastolic blood pressure between the groups.	2) 20 U of oxytocin provided comparable blood loss compared to higher doses with less SBP and DBP decline in the postoperative period.	

Table 2. *AGREE II Tool Collected Results*

		APPRAISER 1	APPRAISER 2	APPRAISER 3	APPRAISER 4	APPRAISER 5	TOTAL
SCOPE AND PURPOSE	Item 1	7	6	6	7	7	33
	Item 2	7	6	6	6	7	32
	Item 3	7	6	6	6	7	32
	Total	21	18	18	19	21	97
CALCULATED DOMAIN SCORES	.9						
STAKEHOLDER INVOLVEMENT	Item 4	7	6	6	6	7	32
	Item 5	7	6	6	6	7	32
	Item 6	6	6	6	6	7	31
	Total	20	18	18	18	21	95
CALCULATED DOMAIN SCORES	.89						
RIGOR OF DEVELOPMENT	Item 7	7	6	7	7	7	34
	Item 8	7	6	7	7	7	34
	Item 9	7	5	6	6	6	30
	Item 10	7	6	6	6	6	31
	Item 11	6	6	6	6	6	30
	Item 12	6	6	6	6	6	30
	Item 13	6	5	6	6	6	29
	Item 14	6	5	6	6	6	29
	Total	52	45	50	50	50	247
CALCULATED DOMAIN SCORES	.9						
CLARITY OF PRESENTATION	Item 15	7	6	7	7	7	34
	Item 16	7	6	7	7	7	34
	Item 17	7	6	7	6	6	32
	Total	21	18	21	20	20	100
CALCULATED DOMAIN SCORES	.94						
APPLICABILITY	Item 18	7	5	7	7	7	33
	Item 19	6	5	7	6	7	31
	Item 20	6	5	7	6	7	31
	Item 21	6	5	7	6	6	30
	Total	25	20	28	25	27	125
CALCULATED DOMAIN SCORES	97						
EDITORIAL INDEPENDENCE	Item 22	6	7	7	7	7	34
	Item 23	6	7	7	7	7	34
	Total	12	14	14	14	14	68
CALCULATED DOMAIN SCORES	.97						
OVERALL GUIDELINE ASSESSMENT		7	6	7	7	6	33
TOTAL OBTAINED SCORES	.93						

Table 3. *PFQ Item Frequency*

	Strongly agree (% of total)	Neither agree or disagree (% of total)	Strongly disagree (% of total)
1. Are you responsible for the care of patients for whom this draft guideline report is relevant? This may include the referral, diagnosis, treatment, or follow-up of patients.	12 (100%)	0 (0%)	0 (0%)
2. The rationale for developing a guideline is clear.	12 (100%)	0 (0%)	0 (0%)
3. There is a need for a guideline on this topic.	9 (75%)	2 (16.67%)	1 (8.33%)
4. The literature search is relevant and complete (e.g., no key evidence was missed, nor any included that should not have been) in this draft guideline.	12 (100%)	0 (0%)	0 (0%)
5. I agree with the methodology used to summarize the evidence included in this draft guideline.	12 (100%)	0 (0%)	0 (0%)
6. The results of the evidence described in this draft guideline are interpreted according to my understanding of the evidence.	12 (100%)	0 (0%)	0 (0%)
7. The draft recommendations in this report are clear.	12 (100%)	0 (0%)	0 (0%)
8. I agree with the draft recommendations as stated.	12 (100%)	0 (0%)	0 (0%)
9. The draft recommendations are suitable for the patients for whom they are intended.	12 (100%)	0 (0%)	0 (0%)
10. The draft recommendations are too rigid to apply to individual patients.	8 (66.67%)	1 (8.33%)	3 (25%)
11. When applied, the draft recommendations will produce more benefits for patients than harms.	10 (83.33%)	2 (16.67%)	0 (0%)
12. The draft guideline presents options that will be acceptable to patients.	11 (91.67%)	1 (8.33%)	0 (0%)
13. To apply the draft recommendations will require reorganization of services/care in my practice setting.	9 (75%)	2 (16.67%)	1 (8.33%)
14. To apply the draft guideline recommendations will be technically challenging.	6 (50%)	2 (16.67%)	4 (33.33%)
15. The draft guideline recommendations are too expensive to apply.	6 (50%)	1 (8.33%)	5 (41.67%)
16. The draft guideline recommendations are likely to be supported by a majority of my colleagues.	10 (83.33%)	1 (8.33%)	1 (8.33%)
17. If I follow the draft guideline recommendations, the expected effects on patient outcomes will be obvious.	10 (83.33%)	2 (16.67%)	0 (0%)
18. The draft guideline recommendations reflect a more effective approach for improving patient outcomes than is current usual practice. (If they are the same as current practice, please tick NA).	11 (91.67%)	0 (0%)	1 (8.33%)
19. When applied, the draft guideline recommendations will result in better use of resources than current usual practice. (If they are the same as current practice, please tick NA).	11 (91.67%)	1 (8.33%)	0 (0%)

20. I would feel comfortable if my patients received the care recommended in the draft guideline.	12 (100%)	0 (0%)	0 (0%)
21. This draft guideline should be approved as a practice guideline.	9 (75%)	2 (16.67%)	1 (8.33%)
22. If this draft guideline were to be approved as a practice guideline, I would use it in my own practice.	12 (100%)	0 (0%)	0 (0%)
23. If this draft guideline were to be approved as a practice guideline, I would apply the recommendations to my patients.	12 (100%)	0 (0%)	0 (0%)

Source: Brouwers, M.C., Graham, I.D., Hanna, S.E., Cameron, D.A., & Browman, G.P. (2004). Clinicians' assessments of practice guidelines in oncology: The CAPGO survey**.** *International Journal of Technology Assessment in Health Care, 20*(4), 421-6.

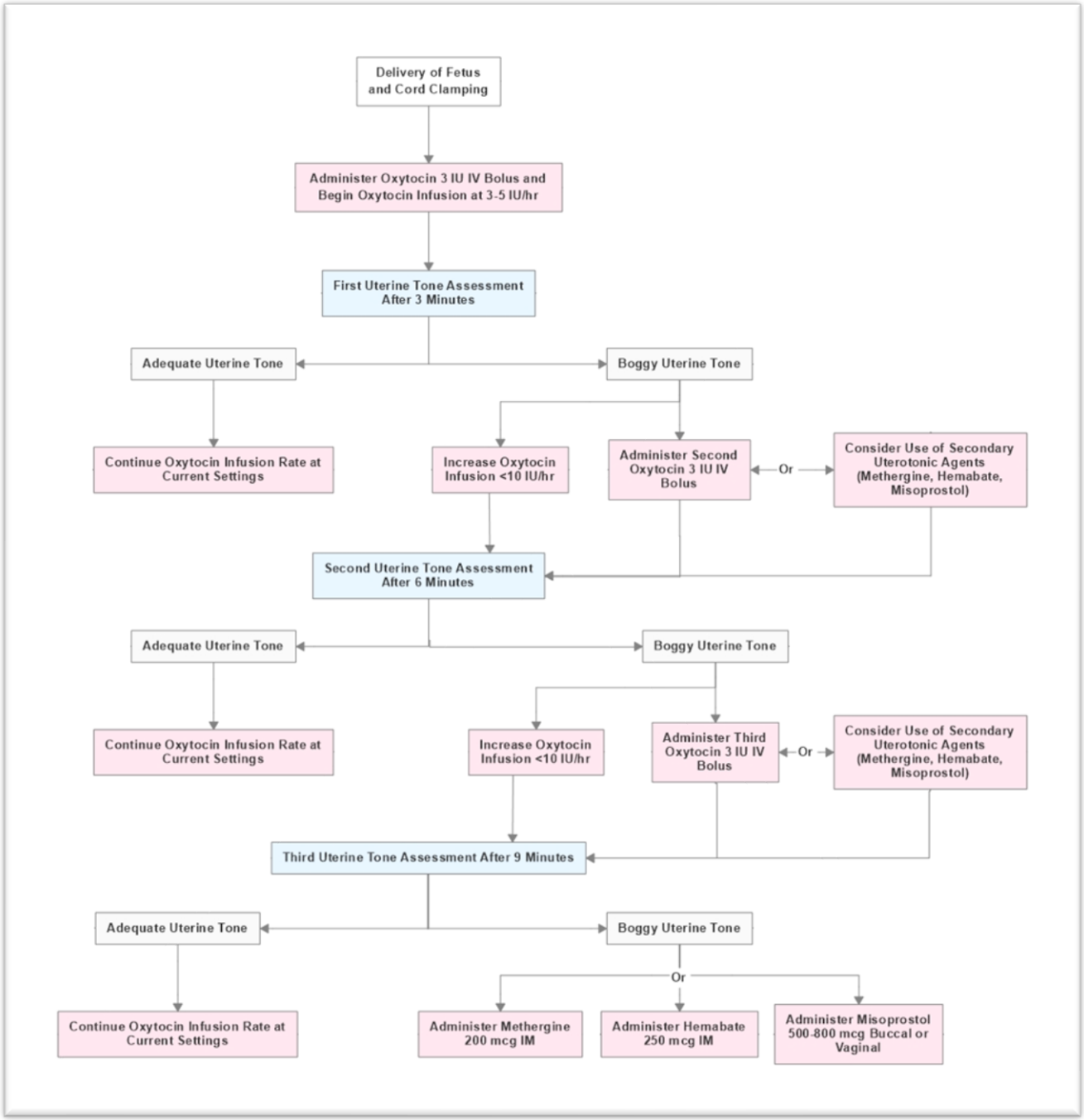

Figure 1. Intraoperative Oxytocin Administration Algorithm

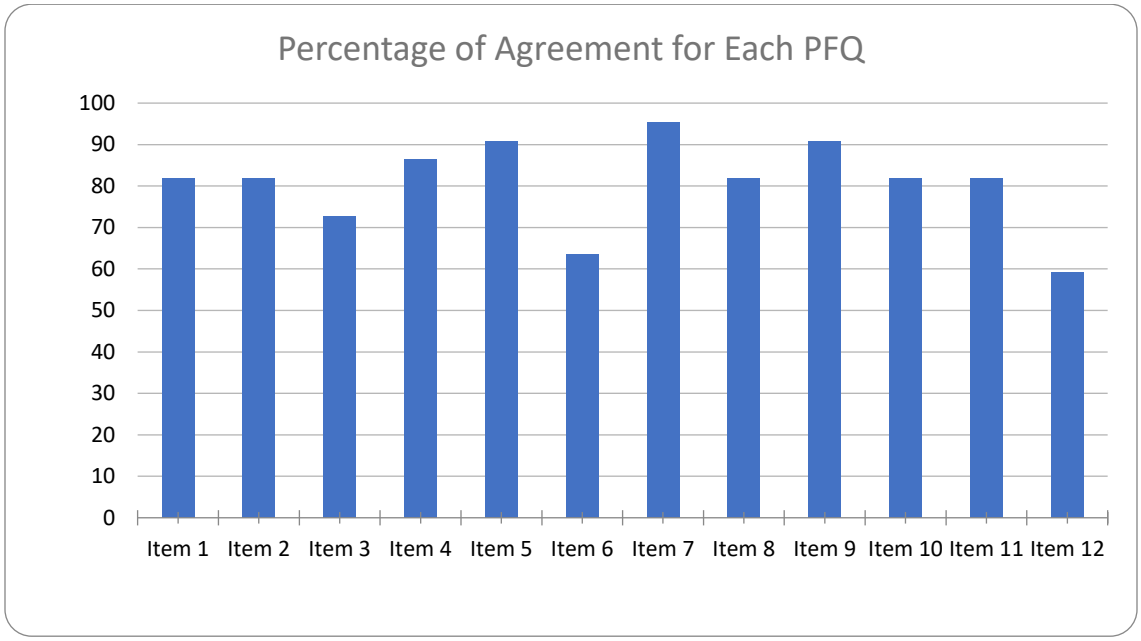

Figure 2. Providers Feedback Questionnaire Results

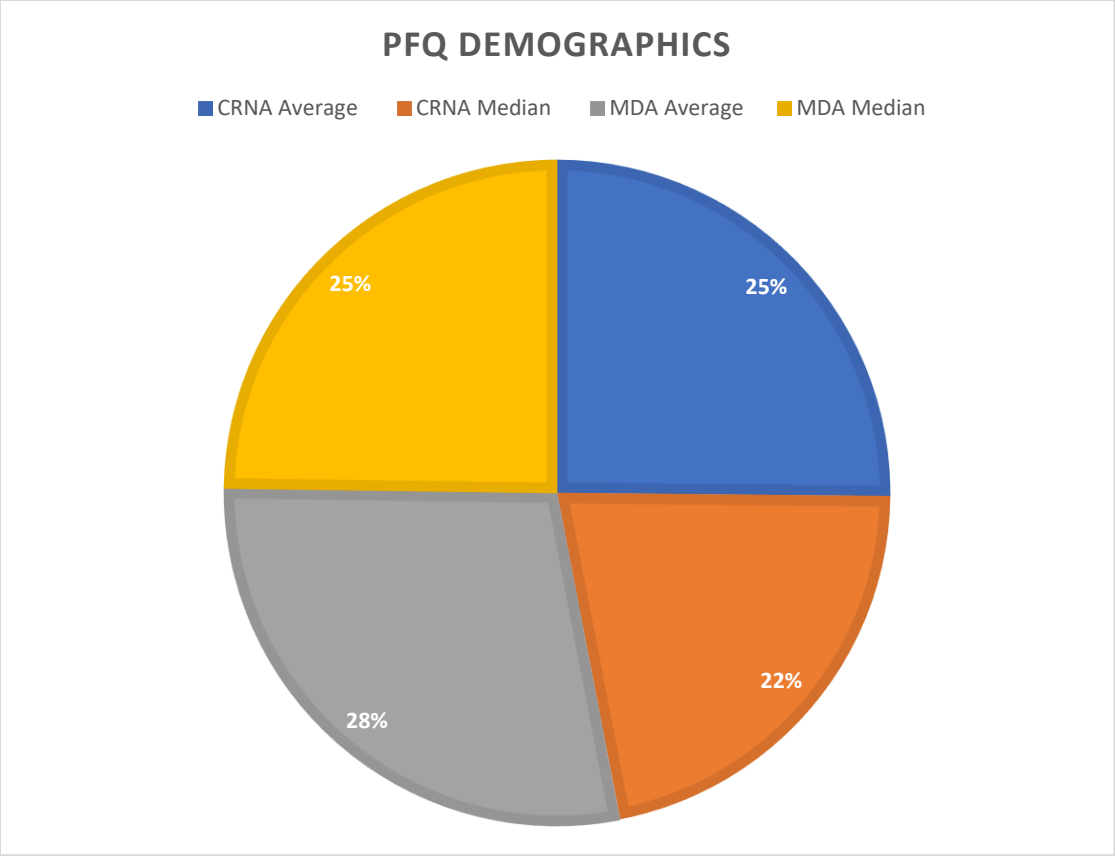

Figure 3. Provider Feedback Questionnaire Demographics

Appendix A
Oxytocin Administration Clinical Practice Guideline

PURPOSE

To implement an evidence based Clinical Practice Guideline (CPG) for oxytocin administration after the delivery of the fetus and cord clamping during elective and non-elective cesarean deliveries for use by anesthesia providers

BACKGROUND

Cesarean deliveries increase the risk for uterine atony and postpartum hemorrhage. Thus, oxytocin is recommended as the "gold standard" to reduce the incidence of uterine atony and postpartum hemorrhage. Once exogenous oxytocin is administered, it will bind to the oxytocin receptors at the uterus and cause uterine contractions. Uterine contractility decreases the incidence of bleeding after the delivery of fetus and cord clamping. However, the lack of a national standard for oxytocin administration has resulted in variability of oxytocin dosing and administration methods (i.e. bolus or infusion) by anesthesia providers at a local Baltimore community hospital. In order to decrease variability and create a standardized practice, a clinical practice guideline will be developed and implemented. The clinical practice guideline is not applicable to emergent cesarean deliveries (i.e. placenta abruption).

IMPLEMENTATION

Preoperative Recommendations

1. Refer to Diagram 1 for "Rule of Three's" Oxytocin Administration Protocol
2. Protocol will be applied to all mothers who are undergoing cesarean delivery: elective and non-elective (i.e. failure to progress or descend after Pitocin induction, urgent cesarean delivery required due to non-reassuring fetal heart tones or loss of variability)
3. Prepare Oxytocin Bolus syringe
    a. One Oxytocin Vial: 10 IU/ mL
    b. Reconstitute three 10mL syringes: Oxytocin 3 IU with 10 mL of sterile 0.9% Normal Saline (final concentration of Oxytocin 0.3 IU/mL)

        OR

    c. Reconstitute one 10ml syringe: Oxytocin 10 IU with 10 mL of sterile 0.9% Normal Saline (Oxytocin 1 IU/mL)
4. Pre-program the Alaris Infusion Pump
    a. Starting Infusion Rate: Oxytocin 50 milliunits/min (~ 3 IU/hr)
    b. Acceptable titration range to achieve adequate control of uterine tone: 50-166 milliunits/min (~5-10 IU/hr)

Intraoperative Recommendations

1. Delivery of Fetus and After 30 seconds of delayed cord clamping→ Administer first bolus dose of Oxytocin 3 IU IV over 45 seconds and begin oxytocin infusion at 50 milliunits/min (~3 IU/ hr)
2. First Uterine Tone Assessment (after three minutes since oxytocin administration): ask obstetrician "how is the uterine tone?"

   a. If response is "good"→ continue oxytocin infusion into perioperative period and follow postoperative recommendations
   b. If response is "boggy"→
      i. Administer second bolus dose of Oxytocin 3 IU over 45 seconds
      AND
      ii. Discuss administration of additional uterotonic agents (ex. Methergine 200mcg IM, Hemabate 250mcg IM, Misoprostol 500- 800 mcg Buccal or Vaginal)
      iii. Titrate Oxytocin infusion to no more than 166 milliunits/min (~10 IU/hr)
      iv. What is the current estimated blood loss?
   c. Monitor for Oxytocin hemodynamic side effects
3. Second Uterine Tone Assessment (after three minutes since first oxytocin administration): ask obstetrician "how is the uterine tone?"
   a. If response is "good" → continue current oxytocin infusion rate into perioperative period and follow postoperative recommendations
   b. If response is "boggy" →
      i. Administer a third dose of Oxytocin 3 IU over 45 second
      AND
      ii. Discuss and consider use of additional uterotonic agents (ex. Methergine 200 mcg IM, Hemabate 250 mcg IM, Misoprostol 500-800 mcg Buccal or Vaginal)
      iii. Monitor for Oxytocin hemodynamic side effects
      iv. What is the current estimated blood loss?
4. Third Uterine Tone Assessment (after three minutes since second oxytocin bolus administration): ask obstetrician "how is the uterine tone?"
   a. If response is "good" → continue oxytocin infusion into perioperative period and follow postoperative recommendations
   b. If response is "boggy" → Discuss with obstetrician and use additional uterotonic agents to obtain adequate uterine tone (ex. Methergine 200 mcg IM, Hemabate 250 mcg IM, Misoprostol 500-800 mcg Buccal or Vaginal)
      i. What is current estimated blood loss?
      ii. What is the hemodynamic status of the patient (stable versus unstable)?
      iii. Was this patient on Oxytocin for trial of labor prior to cesarean section? If so, consider there is a down regulation of receptors and refer to Appendix B for additional uterotonic medications and dosing.
      iv. Does obstetrical hemorrhage protocol need to be activated? If so, communicate with team and refer to Appendix C to follow the institution's Obstetrical Hemorrhage Protocol

Postoperative Recommendations

1. Continue Oxytocin infusion (concentration of 30 IU/500 mL of lactated ringers) at the infusion rate maintained during the cesarean section. May titrate dose based on patient response, but not to exceed 10 U over a 4-hour period.
2. L&D RNs will:

i. Obtain initial assessment of uterine tone and vaginal bleeding assessment upon admission to the PACU
ii. Immediately notify anesthesia and obstetrical providers of inadequate uterine tone or excessive postpartum bleeding
iii. Determination will be made by anesthesia and obstetrical team if the administration of additional uterotonic agents will be needed or obstetrical hemorrhage protocol needs to be activated

Appendix B
Providers Feedback Questionnaire

	Strongly agree	Neither agree or disagree	Strongly disagree
1. Are you responsible for the care of patients for whom this draft guideline report is relevant? This may include the referral, diagnosis, treatment, or follow-up of patients.			
2. The rationale for developing a guideline is clear.			
3. There is a need for a guideline on this topic.			
4. The literature search is relevant and complete (e.g., no key evidence was missed, nor any included that should not have been) in this draft guideline.			
5. I agree with the methodology used to summarize the evidence included in this draft guideline.			
6. The results of the evidence described in this draft guideline are interpreted according to my understanding of the evidence.			
7. The draft recommendations in this report are clear.			
8. I agree with the draft recommendations as stated.			
9. The draft recommendations are suitable for the patients for whom they are intended.			
10. The draft recommendations are too rigid to apply to individual patients.			
11. When applied, the draft recommendations will produce more benefits for patients than harms.			
12. The draft guideline presents options that will be acceptable to patients.			
13. To apply the draft recommendations will require reorganization of services/care in my practice setting.			
14. To apply the draft guideline recommendations will be technically challenging.			
15. The draft guideline recommendations are too expensive to apply.			
16. The draft guideline recommendations are likely to be supported by a majority of my colleagues.			
17. If I follow the draft guideline recommendations, the expected effects on patient outcomes will be obvious.			
18. The draft guideline recommendations reflect a more effective approach for improving patient outcomes than is current usual practice. (If they are the same as current practice, please tick NA).			
19. When applied, the draft guideline recommendations will result in better use of resources than current usual practice. (If they are the same as current practice, please tick NA).			
20. I would feel comfortable if my patients received the care recommended in the draft guideline.			

21. This draft guideline should be approved as a practice guideline.

22. If this draft guideline were to be approved as a practice guideline, I would use it in my own practice.
23. If this draft guideline were to be approved as a practice guideline, I would apply the recommendations to my patients.

Adapted from: Brouwers, M.C., Graham, I.D., Hanna, S.E., Cameron, D.A., & Browman, G.P. (2004). Clinicians' assessments of practice guidelines in oncology: The CAPGO survey**.** *International Journal of Technology Assessment in Health Care, 20*(4), 421-6.