Can Loco-regional Anesthesia With Liposomal Bupivacaine Reduce Intra- and Post-operative Narcotic Use in Patients Undergoing Lower Extremity Revascularization? A Prospective, Triple Blinded, Randomized Trial

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General Study Information

Principal Investigator: Tiziano Tallarita, MD

Co-Investigators: Carmelina Gurrieri, MD; Indrani Sen MBBS, Sai Vang P.A-C, Gloria Krueger P.A-C, Rachel Jack D.N.P, all the research team

Mayo Clinic Health System Region: NWWI

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Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale

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Protocol Summary

Title: Can Loco-Regional Anesthesia with Liposomal Bupivacaine Reduce Intra- and Post-Operative Narcotic Use in Patients Undergoing Lower Extremity Revascularization? A Prospective, Triple Blinded, Randomized Trial

Study Description: *Hypothesis*: Loco-regional injection of liposomal bupivacaine (Exparel solution) as ilio-inguinal block and in the surgical site will reduce intra- and post-operative narcotic use in patients undergoing elective lower extremity revascularizations. To assess the hypothesis, liposomal bupivacaine will be compared to loco-regional injection of normal saline. The study will be randomized and triple blinded.

Objectives: *Primary objectives*: 1) reduce intra- and post-operative narcotic use; 2) improve patient recovery experience.

Secondary objectives: 1) Allow early ambulation after surgery by better pain control; 2) decrease hospital stay.

Endpoints:

Primary endpoints:

1. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block + injection in the surgical wound) with liposomal bupivacaine injection reduces the postoperative use of narcotics at 12, 24, 48 and 72 hrs after the injection, when compared with normal saline injection (control group).
2. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block + injection in the surgical wound) with liposomal bupivacaine injection reduces postoperative use of narcotics at 30 days, when compared with normal saline injection (control group).

Secondary Endpoints:

1. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block) with liposomal bupivacaine injection improves postoperative quality of recovery assessed at 14 and 28 days, compared to normal saline injection (control group).
2. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block) with liposomal bupivacaine injection reduces the intraoperative use of narcotics, when compared with normal saline injection (control group).
3. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block) with liposomal bupivacaine injection reduces length of hospital stay, when compared with normal saline

injection (control group).

Study Population:	20 patients, ≥18 years old, both genders, in the Wisconsin area (rural and non-rural), affected by chronic peripheral arterial disease of the lower extremity.
Phase:	N/A
Description of Sites/Facilities Enrolling Participants:	This will be a single site only (Mayo Clinic Health System in Eau Claire), enrolling local patients (Wisconsin rural and non-rural areas) with lower extremity, chronic atherosclerotic disease requiring intervention.
Description of Study Intervention:	It will be a triple blinded, controlled randomized trial assessing potential reduction in narcotic use in patients undergoing lower extremity revascularization, when loco-regional anesthesia with liposomal bupivacaine solution is performed, compared to normal saline injection. Loco-regional anesthesia for lower extremity revascularization will include an ultrasound guided ilio-inguinal block with Exparel solution and local injection in the wound(s) edges of more liposomal bupivacaine solution. The control group will receive injection of normal saline instead. Lower extremity revascularizations will include femoral endarterectomy with patching ± antegrade or retrograde endovascular intervention (one or more combination of stenting, atherectomy, balloon angioplasty) or bypass (femoral popliteal or femoral tibial bypasses with vein or prosthetic graft).
Study Duration:	Total time to data analysis will be around 8 months
Participant Duration:	Enrollment will be for a 6 month period. Each patient will be followed for 28 days.

Schedule of Assessments

	Enrollment	Hospital Stay			48 hrs post op	72 hrs post op	14 days post op	28 days post op
		Procedure	Recovery	Discharge				
		Day 1			Day 2 ± 1 day	Day 3 ± 1 day	Day 14 ± 2 days	Day 28 + 4 days
Informed Consent	x							
Randomization	x							
Demographics	x							
Medical history	x							

Medication Review	x							
Study Treatment		x						
Pain Score			x	x	x	x	x	x
QoR-15	x			x				x
Urine Drug Screen							x	x
Adverse Events		x			x	x	x	x
Phone Call					x*	x*		x
Clinic Visit	x						x	

* If participant has been discharged.

Research Question and Aims

Hypothesis: Local regional anesthesia with liposomal bupivacaine injection does reduce intraoperative and postoperative narcotic use in patients undergoing lower extremity revascularizations.

Aims, purpose, or objectives: Complete a triple blinded randomized trial comparing loco-regional liposomal bupivacaine injection versus normal saline (placebo control group) to assess possible reduction of intra- and post- operative narcotic use (and improve patient recovery experience) with liposomal bupivacaine, in patients undergoing lower extremity revascularization.

Background:
Fighting narcotic abuse has been a national mission for many years.

The use of opioids including prescription drugs and heroin, has reached epidemic levels. Overdoses from opioids have become the leading cause of death in Americans surpassing cancer, and traumatic deaths. In 2017, 72,000 Americans were killed by opioid overdoses, more losses than in both the Vietnam and Iraq wars. The prescription of opioids by physicians to manage postoperative pain has been identified as one of the factors contributing to this epidemic.

Regional anesthesia has been shown to decrease the use of postoperative narcotics and improve early mobilization and overall patient's satisfaction in nonvascular abdominal and inguinal surgeries.1-9 As result, ultrasound guided regional anesthesia of the abdomen (transversus abdominis plan block) with liposomal bupivacaine is becoming standard of care in several types of abdominal surgeries (for oncological, gynecological, or urological surgical diseases, as few examples).

Ilioinguinal block has been proved to be effective in minimizing narcotic use and improving early postoperative activity after inguinal hernia repair. 1-3

To our knowledge, there have not been studies (retrospective or prospective) addressing the effectiveness of a regional/local anesthesia with ilio-inguinal block using liposomal bupivacaine in patients undergoing lower extremity revascularizations.

Risk/Benefit Assessment:
Twenty cc of Liposomal bupivacaine is mixed to 30 cc of regular bupivacaine 0.25% and 100 cc of normal saline. Thirty cc of this mix is injected in the transversalis abdominis plan (TAP block) before making the incision. The rest of the mix is injected locally (that is why is called "loco-regional" anesthesia) once the surgical wound is created. The injection of normal saline (control group) is also safe because normal saline has been already used in the Liposomal bupivacaine mix, without causing reactions/side effects or any other complications.

Currently, there are no clear guidelines regarding how to treat post-op pain in patients undergoing lower extremity revascularization. New guidelines are about to be published that mention the use of multimodal pain control (which is extrapolated from the literature of non-vascular procedures), including regional anesthesia. But it is not very clear what they mean for regional anesthesia, vaguely mentioning a small trial of femoral/sciatic nerve block as the only source of this statement. In fact, there are no studies of this kind for patients undergoing lower extremity revascularization. The femoral/sciatic nerve block is a deep block that causes both sensory and motor paralysis. In addition, because the nerves are deep, there is a higher risk of complications. That is the reason it is not utilized.

Because of this huge gap in the literature, one of the secondary aims of this study is to provide a benchmark for future guidelines on pain control in vascular patients.

Study Design and Methods

This will be a single site (Mayo Clinic Health System in Eau Claire), triple blinded, controlled randomized trial assessing potential reduction in narcotic use in patients undergoing lower extremity revascularization, when loco-regional anesthesia with liposomal bupivacaine solution (mixed to normal saline and 0.25% bupivacaine) is performed, compared to normal saline injection. Lower extremity revascularizations will include femoral endarterectomy with patching ± antegrade or retrograde endovascular intervention (one or more combination of stenting, atherectomy, balloon angioplasty) or bypass (femoral popliteal or femoral tibial bypasses with vein or prosthetic graft). The case volume of the two surgeons involved in the study is about 100 cases/year of elective open or hybrid lower extremity revascularizations.

Recruitment:

Each patient candidate for elective lower extremity revascularization (seen during a standard vascular surgery consult), will be asked if he/she wants to participate in the research study, after the main details of the study will be explained to the patient. If a patient is interested in the study, the research team will step in, discuss more in detail the study, and possibly obtain consent.

Consenting Procedure:

Before any procedure is performed, informed consent will be obtained.

A single informed consent form that describes both the study procedures will be discussed with the patient including pros and cons of injection of liposomal bupivacaine or normal saline, side effects and potential complications of these medications.

Patients need to agree to perform a urine drug test at 14 and 28 days if required (see below), complete the survey questionnaire for patient's recovery satisfaction and provide the highest pain score.

The attending provider or the team nurse practitioner, resident or research coordinator will obtain the consent. These individuals would have basic medical education and degree necessary for proper explanation of the details of the study and the medical implications involved. Patients will be reconsented if needed after any major change in clinical condition or adverse events reporting. A copy of the signed informed consent will be kept in the medical record and a digital copy maintained on a password protected secure file.

At the time of the signature of the consent, the patients will receive educational materials regarding use of narcotics and associated side effects, covering the main points showed in the attachment 3.(10,11) The educational material on narcotic use will be re-discussed with the patients at the time of the discharge.

Randomization

Patients will be randomized following consent and subsequently evaluated with intention to treat. Randomization will be performed by the research coordinator. The research coordinator team will be in charge of randomizing patients. The randomization will be done with REDCap and the assignment will be emailed to the pharmacy, maintaining the blinding of the study. Based on the emailed assignment, pharmacy will send the solution (either liposomal bupivacaine or normal saline) to inject during the ultrasound guided ilio-inguinal block.

Patient, surgeon, and the team assessing the patient postoperatively will be blinded (triple blinded). Normal saline or liposomal bupivacaine mix will be "blinded" by using a covered syringe, to keep the surgeon unaware of what he/she is injecting. The patient will be blinded as well, as the solution injected (liposomal bupivacaine versus normal saline) will not be charged to the patient's bill.

Intervention

At the day of surgery, the enrolled patients will be medicated in pre- and intra-operative phases by the anesthesia team in a standardized fashion, based on the protocol in **attachment 4**. The surgeon will, instead, perform the loco-regional anesthesia with the liposomal bupivacaine/bupivacaine/normal saline mix (or normal saline alone).

Treatment technique:
The patient will be brought to the operative room and general anesthesia initiated in supine position. After the patient will be prepped and draped in standard sterile fashion, the new intervention, for which this study is designed, will include identifying the transversus abdominis muscle with ultrasound guidance, few centimeters above the anterior superior iliac spine, in the surgical side. Using sterile technique, an 20g Nerve block needle will be inserted and advanced under ultrasound guidance until it is below the fascial covering of the transversus abdominis muscle layer. Gentle aspiration for air, or blood will be performed and either 30 mLof a mix with 1

vial of 20 cc of Liposomal bupivacaine+1 vial of 30 cc of 0.25% bupivacaine+100 cc of saline or 30 mL of normal saline alone (control group)will be injected under ultrasound guidance . For each 5cc of local anesthetic injected, aspiration will be performed. Upon completion of the injection, the needle will then be removed. In the control group, the same technique will be utilized but normal saline alone will be injected instead. The type of solution injected will be hidden by using a covered syringe that does not show the color of the solution inside, to keep the surgeon blinded. Both the patient and the surgeon will not be aware of the solution injected.
During the procedure, after the plan of dissection is completed and the target vessels exposed and controlled, the edges of the wound(s) will be injected with the remaining mix of Liposomal bupivacaine/bupivacaine/normal saline (or normal saline alone in the control group). The surgical revascularization will continue as per standard of care. At the end of the revascularization, the wound(s) will be closed in multiple layers. Once the procedure is completed, the patient will be sent to the recovery room and eventually to the hospital room.

During the inpatient hospital phase of their recovery patients will be assessed by the rounding team for pain score and postoperative complications. After the surgery is completed, the rounding team will evaluate the patient for signs of complications (based on the Clavien–Dindo grading system; figure 1) and ask the patients their minimum and maximum pain score (reported as 0-10 verbal numerical rating scale with 10 being worst pain) in the first 72 hours. The assigned nurse will also assess patient's pain with the Visual Analogue Score (VAS; Figure 1). If VAS is >3 after the non-narcotic medications have been given, oral or intravenous narcotic medication will be administered.
The nurse(s) taking care of the study patients will fill a specific form (attachment 1) every time a narcotic medication is administered, specifying the pain score at the time of the administration and the location of the pain. The filled form will be handed to the rounding team on a daily basis.
Discharge criteria include pain <4/10, independence of intravenous analgesia, and being medically stable for discharge. If patients are waiting for placement, the time of discharge for the purpose of the study will be the day they have met such criterion as opposed to the day of actual discharge, as this can vary depending on patient placement.

If a patient is discharged before 72 hours, the team will call the patient at 48 and 72 hours to assess pain score. The maximal pain score value for the time period 0-72 hours will be chosen as the maximal pain during that time period.

Demographics, pre-operative cardiovascular risk factors, procedural details, intra- and post-operative complications, hospital stay, patient recovery satisfaction, intraoperative narcotic use (in morphine equivalent), postoperative narcotic use (in morphine equivalent) at 12, 24, 48, and 72hr, total postoperative narcotic use (in morphine equivalent) at 28 days after the ilio-inguinal block will be recorded in a REDCap database.
The amount of postoperative narcotic use will be calculated in morphine equivalent. Inpatient narcotic use will be extrapolated from the patient's chart and the nursing forms. Outpatient narcotic use will be based on the narcotic prescription(s) filled by the patient. A urine drug screen will be obtained at 14 days (at the time of the first postoperative clinic visit) and at 28 days, but only in those patients who did not fill the narcotic prescription, to make sure those patients did not obtain narcotics from other sources.

Patient quality of recovery and satisfaction will be assessed with a patient survey administered prior to surgery as a baseline, the day of discharge, and at 28 days (see attachment 2). For quality of recovery measurement, we used the validated and

psychometrically evaluated questionnaire QoR-15 from Stark and colleagues, a short form of the comprehensive 40-item questionnaire QoR-40. (12,13).

Follow-up Visits
Following discharge patients will be seen in clinic at 14 days for wound check, pain control, patient's recovery satisfaction and narcotic use. Treatment administration form, vitals, and adverse events will be reviewed at follow-up appointment. If no narcotic prescription has been filled until then, a urine drug test will be administered to make sure the patient did not take narcotic medication from other sources.

At 28 days, a phone call follow up will be performed to check wound(s), pain control, recovery satisfaction and narcotic use. If no narcotic prescription has been filled, a urine drug test will be administered to make sure the patient did not take narcotic medication from other sources.

Subject Information

Target accrual: 20 participants

Subject population: Those who meet inclusion/exclusion criteria in the Wisconsin area (rural and non-rural), affected by chronic peripheral arterial disease of the lower extremity.

Inclusion Criteria:

- ≥ 18 years of age
- All males
- Females if sterile (history of tubal ligation or hysterectomy) and/or last menses was > 1 year ago.
- Elective lower extremity revascularization is scheduled or being scheduled.

Exclusion Criteria:

- Non-English speaking
- Chronic pain, currently requiring opioids
- On opioids greater than 1 weeks
- Allergy to local anesthetics
- Use of spinal or epidural for surgery
- Lack of patient cooperation
- Contraindication to regional anesthesia
- Vulnerable individuals
- Urgent/emergent surgeries
- Known to be pregnant or able to become pregnant.

Review of medical records, images, specimens

The study involves data that exists at the time of IRB submission and data that will be generated after IRB submission.

Data and Safety Monitoring Plan

Subject Safety:
Mayo Clinic requires a basic level of research training for all Investigators and research personnel involved in human subject research regardless of the source of funding. Investigators and personnel who participate in the design, conduct, or reporting of research involving human subjects at Mayo Clinic must complete training in protecting human research participants. All study team members must have completed the Mayo Clinic Human Subject Protection initial training.

The enrolled patients will be medicated in pre- and intra-operative phases by the anesthesia team in a standardized fashion, based on the protocol in **attachment 4**. The treatment technique will be followed as described in this protocol. The rounding team will evaluate the patient for signs of complications and ask the patients their minimum and maximum pain score according to the schedule outlined in the methods.

Mental Health Mitigation Plan:
Study staff will review the QoR-15 questionnaire completed by each participant. If the participant indicates feeling anxious or depressed all of the time (score 0-1), staff will inform the Principal Investigator. The investigator will respond with a referral to psychology. If the participant is unable to attend an appointment, the investigator will contact the primary care provider of the participant.

Data Integrity:
All participant data relating to the study will be recorded on electronic case report forms (eCRFs) using an application such as REDCap. The Investigator is responsible for verifying that data entries are accurate and correct. All data will be entered into a password protected database. There will be manual quality checks that will occur during the data collection and analyses process to ensure it is accurate and complete. The data will be monitored regularly for accuracy and a formal policy regarding protection of personal privacy is in place throughout Mayo Foundation.

Subject Privacy:
Prior to interactions, in person and virtually, participants will be asked to verify their identity with two personal identifiers. The consent visit will be done in a private office at the clinic or virtually using approved technology provided by Mayo Clinic.

Data Confidentiality:
Information about the study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Access to the EDC system is limited to study staff and requires a secure username and password. Clinical information will not be released without permission of the participant, except as necessary for monitoring by the FDA or other applicable regulatory authorities.
To maintain confidentiality, all evaluation forms, reports and other records will be identified by a unique identifier.
The investigator will maintain a log to connect the unique identifier to the participant. This log will be kept on a Mayo Clinic server which limits access to the designated study team. Any data recorded on paper will be stored

in locked file cabinets in secure offices on the Mayo Clinic campus.

Product Accountability:
Investigational Product(s) (IP) are received by study personnel acting on behalf of the investigator. Research pharmacy staff are responsible for obtaining, storing, preparing, and disposing of the study drug.

Study Documentation:
The Investigator must maintain accurate documentation (source data) that supports the information entered in the eCRF including description of procedures for the identification of data to be recorded directly on the eCRF considered as source data. The study team will ensure that the source data are attributable, legible, contemporaneous, original, accurate, and complete whether the data are hand-written on paper or entered electronically.

Study Coordination:
Study coordinators will be assigned tasks by the Principal Investigator as indicated in the Delegation Log. Completion of required training will be documented in appropriate Training Logs. Communication between the investigator and the study team will be done in person and/or by email.

The lead coordinator will maintain a log of Principal Investigator Decisions. They will ensure that all changes/modifications/amendments will be distributed to the study team and document any relevant training requirements associated with them.

Clinical Monitoring:
The investigators and co-investigators will allocate adequate time for such monitoring activities. The investigators and co-investigators will also ensure that the monitor or other compliance or quality assurance reviewer is given access to all the study-related documents and study related facilities (e.g. pharmacy, diagnostic laboratory, etc.), and has adequate space to conduct the monitoring visit. As a service to the sponsor-investigator, this study may be monitored during the conduct of the trial by staff from the Mayo Clinic Office of Research Regulatory Support. Clinical trial monitoring may include review of the study documents and data generated throughout the duration of the study to help ensure the validity and integrity of the data along with the protection of human research subjects. This will assist sponsor-investigators in complying with Food and Drug Administration regulations.

Adverse Events and Serious Adverse Events:
Definition:
Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related. An adverse event (AE) or suspected adverse reaction is considered "serious" if, in the view of the investigator, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization,

or the development of drug dependency or drug abuse.

The following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious."

All adverse events (AEs) must have their relationship to study intervention assessed by the clinician who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be suspect.

- **Related** – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.
- **Not Related** – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

The principal investigator will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and/or phone calls.

Reporting:
The following events require reporting to the IRB withing 5 working days of learning of the event:

- Internal adverse events that are serious; unanticipated, and related to the research (i.e., Unanticipated Problems Involving Risk to Subjects or Others – UPIRTSO);
- Major deviations from the approved research protocol or plan that placed subjects or others at an increased risk of harm
- Significant New information that requires urgent action and/or notification of subjects;
- Breach of confidentiality or violation of HIPAA;
- Incarceration of a research subject;
- Any change to research activity which were made in order to avoid apparent immediate hazards to a subject and were implemented prior to IRB approval.
- PI Administrative Holds

Data Analysis

Power Statement: This will be a Pilot study and will include a small number of participants (N~20)

Data Analysis Plan: Continuous variables will be presented as mean ± SD or as median (interquartile range), while categorical data will be expressed as counts. Continuous numeric variables will be compared using Student's t-test for paired samples or the Wilcoxon test according to their distribution (assessed using the D'Agostino-Pearson test). The threshold of statistical significance was $p \leq 0.05$.

Outcomes:

Primary outcomes:

1. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block) with Exparel injection reduces the postoperative use of narcotics at 12, 24, 48 and 72 hrs after the injection, when compared with normal saline injection (control group).
2. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block) with Exparel injection reduces postoperative use of narcotics at 30 days, when compared with normal saline injection (control group).

Secondary Outcomes:

1. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block) with Exparel injection improves postoperative quality of recovery assessed at 14 and 28 days, compared to normal saline injection (control group).
2. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block) with Exparel injection reduces the intraoperative use of narcotics, when compared with normal saline injection (control group).
3. to determine if loco-regional anesthesia (ultrasound-guided ilio-inguinal block) with Exparel injection reduces length of hospital stay, when compared with normal saline injection (control group).

References

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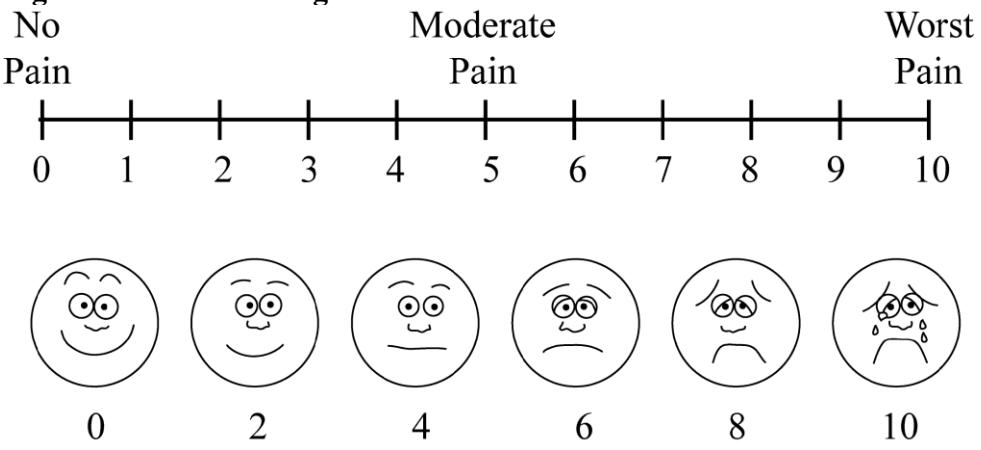
Figure 1: Visual Analogue Score

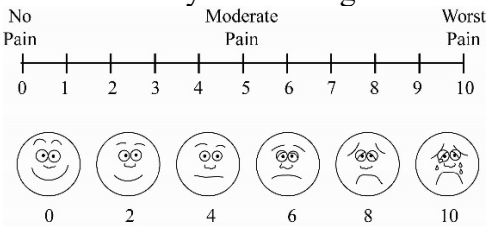


<u>Attachment 1: Nursing form to be filled every time patient is provided with narcotic medication</u>

Nursing Form:

■ Patient: First and last name
■ Age:
■ Date of surgery: mm/dd/yyyy
■ Location of pain:
■ Is the pain located in the surgical site? YES / NO
■ Patient pain score from 0-10:

■ Pain score by nurse using the Visual Analogue Score 0-10 (see below):



■ Was the non-narcotic medication given before the narcotic? YES / NO
If no, what was the reason for no giving it? Explain:
■ Narcotic given: Name:……..dosage:…….Time ..... am/pm
■ Pain score at one hour after the narcotic was given: 0-10
■ Printed name of the nurse: ……
■ Signature ..... Date: mm/dd/yyyy

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Attachment 2: Patient satisfaction survey based on 15 questions

QoR-15 Patient Survey

Date: _ _ / _ _ / _ _ Study #: _____

Preoperative ☐ Postoperative ☐

PART A

How have you been feeling in the last 24 hours?

(0 to 10, where: 0 = none of the time [poor] and 10 = all of the time [excellent])

1. Able to breathe easily	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
2. Been able to enjoy food	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
3. Feeling rested	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
4. Have had a good sleep	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
5. Able to look after personal toilet and hygiene unaided	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
6. Able to communicate with family or friends	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
7. Getting support from hospital doctors and nurses	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
8. Able to return to work or usual home activities	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
9. Feeling comfortable and in control	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
10. Having a feeling of general well-being	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time

PART B

Have you had any of the following in the last 24 hours?

(10 to 0, where: 10 = none of the time [excellent] and 0 = all of the time [poor])

11. Moderate pain	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time
12. Severe pain	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time
13. Nausea or vomiting	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time
14. Feeling worried or anxious	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time
15. Feeling sad or depressed	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time

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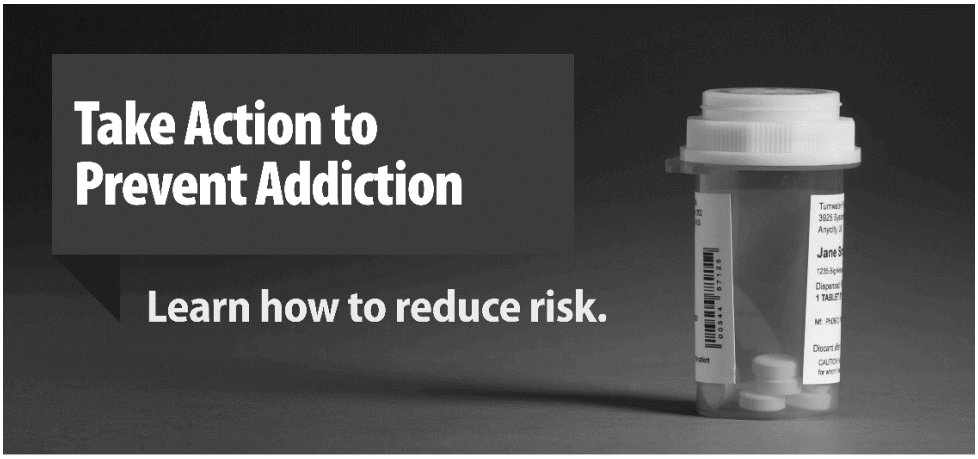
Attachment 3: Patient's education material for narcotic use



Know the Facts About Opioids

41 PEOPLE DIE EVERY DAY

Every day in the United States, 41 people lose their lives to prescription opioid overdose.

Prescription opioids—like hydrocodone, oxycodone, and morphine—can be prescribed by doctors to treat moderate to severe pain but can have serious risks and side effects.

ANYONE CAN BECOME ADDICTED

Opioids are highly addictive. Research shows that if you use opioids regularly, you may become dependent on them.

That's because opioids change how the brain and nervous system function. **You can't know how your brain will react to opioids before taking them.**

Talk With Your Doctor

Your doctor may talk to you about prescription opioids for pain treatment. Ask about the risks and benefits so that you can work together to decide what is best. You can also ask your doctor to help you find other safer ways to manage pain.

It Only Takes a Little to Lose a Lot

Opioids can be addictive and

Opioids affect the part of the brain that

Combining opioids with alcohol and

MAYO CLINIC

Figure 1: Clavien-Dindo classification for postoperative complications

Table 1: Clavien-Dindo classification.

Grades	Definitions of grades	Modes of therapy
Grade I	Any deviation from the normal postoperative course.	No pharmacological or surgical treatment, endoscopic or radiological interventions were required. Acceptable therapeutic regimens are drugs such as anti-emetics, antipyretics, analgesics, diuretics, and electrolytes and physiotherapy. Wound infections or small abscess requiring incision at bedside is within this category.
Grade II	Normal course altered	Pharmacological management other than in Grade 1. Blood transfusions and total parenteral nutrition are also included.
Grade III	Complications that require intervention of various degrees	Sub-classified into: Grade IIIa – complications that require an intervention performed under local anaesthesia. Grade IIIb – interventions that require general or epidural anaesthesia.
Grade IV	Complications threatening life of patients (including CNS complications), requiring ITU support	Further sub-classified into: Grade IV a – single organ dysfunction (including dialysis). Grade IV b – multi-organ dysfunction.
Grade V	Death of a patient	

Attachment 4: Pre- and Intra-operative Anesthesia Management Protocol

1. Preoperative
    - Acetaminophen 1000 mg PO
    - Consider aprepitant 40 mg PO if history of severe PONV (postoperative nausea-vomiting)
    - Avoid scopolamine patch
2. General anesthesia with endotracheal intubation
3. Intravenous analgesia
    - Fentanyl
    - Induction and maintenance dose at discretion of anesthesiologist
    · Limit total intraoperative dose <250 mcg
    - Acetaminophen 1000 mg IV, if > 6 hours from preoperative dose
    - Dexamethasone 4-8 mg IV prior to incision
    - Hydromorphone
        - Only if despite all the prior interventions, patient exhibits signs of "inadequate analgesia" (refractory hypertension, tachycardia, patient movement, etc). Limit total intraoperative dose <1 mg. Check with the anesthesiologist before administering it.

    - Ketorolac 7.5-15 mg IV at closure (discuss it with both anesthesiologist/ surgeon prior to administration)
        - Age > 70 or CrCl < 30 ml/min or Cr > 1.5 = NONE
        - Age 65-69 or weight < 50 kg or CrCl 31-50 ml/min or Cr 1.1-1.5 = 7.5 mg IV
        - Age < 65 or weight ≥ 50 kg or CrCl > 50 ml/min or Cr ≤0 = 15 mg IV

4. No intravenous sedation/analgesia adjunct infusions (dexmedetomidine, ketamine)
5. Anti-emetics
    - Decadron 4 mg IV prior to incision
    - Zofran 4 mg IV at closure