

BIOGRAPHICAL SKETCH

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NAME: Brendan Carvalho

eRA COMMONS USER NAME (credential, e.g., agency login): **B.CARVALHO**

POSITION TITLE: Professor, Vice Chair of Faculty Development and Chief of the Obstetric Anesthesiology and Maternal Health in Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of the Witwatersrand, South Africa	MBBCh	12/94	Medicine
Royal College of Anaesthetists, UK	Resident	10/00	Anesthesiology
Plymouth University, UK	Diploma	08/01	Clinical Research
Stanford University, USA	Fellow	10/22	Obstetric Anesthesiology
American Board of Anesthesiology, USA	Diplomate	10/14	Anesthesiology
American Society of Anesthesiologist (ASA), USA	FASA	07/21	Anesthesiology

A. Personal Statement

I am currently Professor, Vice Chair of Faculty Development, and Chief of the Obstetric Anesthesiology and Maternal Health in the Department of Anesthesiology, Perioperative and Pain Medicine at Stanford University. I am a fellowship-trained Obstetric Anesthesiologist and Regional Anesthesia and Acute Pain Medicine specialist. As a clinician and translational scientist, I have spent the past two decades advancing the care we provide women during and after childbirth. I have the training, expertise, mentorship experience, non-clinical time and motivation necessary to successfully support the proposed project.

I have published extensively in the field of Obstetric Anesthesia with over 350 peer-reviewed articles, editorials, reviews, book chapters and commentaries. My academic focus has centered around clinical and translational research studies, and I have lead and supported many maternal drug and device development projects.

As Vice Chair of Faculty Development and Chief of the Obstetric Anesthesiology and Maternal Health at Stanford, and nationally as Past President of the Society of Obstetric Anesthesia and Perinatology (SOAP), Chair of the SOAP Centers of Excellence, Committee roles at American Society of Anesthesiologists (ASA), California Society of Anesthesiologists (CSA) and World Health Organization (WHO), I have gained the necessary experience, leadership and administrative skills to successfully support this proposed collaborative research project. I have a long track record of successful mentorship of trainees and junior faculty, and oversee the department's Anesthesia Mentorship Program (AMP) and helped develop the SOAP Mentorship Academy. I have led and mentored the world's most academically-productive Obstetric Anesthesia division's research efforts for the past two decades. I have won the SOAP Best Scientific Paper award on 3 occasions, and my trainee-mentored research has been recognized with 14 SOAP Gertie Marx winner/finalists awards.

My biggest research and scholarly contributions have focused around peripartum pain, perinatal pharmacology, and postpartum recovery. I have helped develop devices to assist epidural placement and measure pain objectively, and studied devices to monitor pregnant and postpartum women. I have conducted numerous peripartum drug studies, as well as pharmacokinetic and pharmacodynamic studies to optimize drug dosages and treatment protocols. I understand the importance of the proposed research on a national and global scale, and offer my full effort and support behind the research project.

Ongoing and recently completed projects that I would like to highlight include:

Ongoing:

FAER MRTG MRTG-02-15-2022-Ansari (Jessica)/co-I

07/01/2022-6/30/2024

Calcium chloride for the prevention of blood loss during intrapartum cesarean delivery: a single center randomized controlled trial with nested pharmacokinetic and pharmacodynamic study

A randomized placebo-controlled study to determine if calcium chloride (a repurposed drug that our pilot study showed to be effective) can prevent and treat uterine atony, and reduced obstetric hemorrhage.

CereVu Medical (Carvalho)/PI

04/08/2022-10/31/2023

Evaluation of Objective Pain Measurement Device

The study aims to develop a device to objectively measure pain in laboring mothers that can be applied to a setting when pain cannot be reported e.g. patient under anesthesia or sedation.

Past (selected):

NIH 1R41HD088137-01 (Argun, Giner Inc.)/Site PI

04/01/2016-03/30/2018

Non-Invasive, Highly Specific Detection of Oxytocin in Biological Fluids

A study to develop a point-of-care instrument that would accurately determine the peripheral levels of oxytocin in pregnant women to guide oxytocin administration.

NIH/NICHD R01 HD070795-01A1 (Peltz, Drover)/Co-I

07/12/2012-05/31/2017

Ondansetron to Prevent Neonatal Narcotic Abstinence Syndrome

A study to determine the efficacy of ondansetron to prevent or reduce neonatal narcotic abstinence syndrome in neonates born to women abusing opioids during pregnancy.

NIH K12 BIRCWH mentored research training grant (Carvalho)/PI

07/01/2006-06/30/2009

Acute and Chronic Persistent Pain Following Cesarean Delivery: The role of cytokines

A translational study that developed a cesarean delivery wound-site sampling technique to determine the role of wound biochemical inflammatory mediators in postoperative pain and opioid consumption.

Selected relevant publications (from over 230 peer-reviewed publications)

Brookfield KF, Elkomy M, Su F, Drover DR, **Carvalho B.** Optimization of Maternal Magnesium Sulfate Administration for Fetal Neuroprotection: Application of a Prospectively Constructed Pharmacokinetic Model to the BEAM Cohort. *J Clin Pharmacol.* 2017;57(11):1419-1424. PMID: 28589614

Riley ET, **Carvalho B.** The Episire syringe: a novel loss of resistance syringe for locating the epidural space. *Anesth Analg.* 2007;105(4):1164-6. PMID: 17898406

Weiniger CF, Akdagli S, Turvall E, Deutsch L, **Carvalho B.** Prospective Observational Investigation of Capnography and Pulse Oximetry Monitoring After Cesarean Delivery With Intrathecal Morphine. *Anesth Analg.* 2019;128(3):513-522. PMID: 29958217

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments:

2001-2002 Obstetric Anesthesia Fellowship, Department of Anesthesia, Stanford University
2003-2010 Assistant Professor, Medical Center Line, Department of Anesthesiology, Stanford University
2011-2015 Associate Professor, Medical Center Line, Department of Anesthesiology, Stanford University
2013- Chief, Division of Obstetric Anesthesiology and Maternal Health, Stanford University
2015- Professor, University Medical Center Line, Department of Anesthesiology, Stanford University
2017-2018 President, Society for Obstetric Anesthesia and Perinatology
2022- Vice Chair, Faculty Development, Department of Anesthesiology, Stanford University

Other Experience and Professional Memberships (Selected):

2023- **ACOG** (American College of Obstetricians and Gynecologists) Alliance for Innovation on Maternal Health (**AIM**) Severe Maternal Morbidity Review Form Committee
2022- **GEDSA** (Global Enteral Device Supplier Association), NRFit (neuraxial) Clinical Advisory Board
2022- **SOAP** Mentoring Academy Mentor
2022- **SOAP** Outreach California State Obstetric Anesthesiologist Representative
2021- **ASA** (American Society of Anesthesiologists) Premier Inc's Maternal/Infant Advisory Panel
2021- **ASA** Educational Track Subcommittee, Vice Chair
2021- **CSA** (California Society of Anesthesiologists) District 3 Delegate
2020- **SOAP** Multicenter Research Network Subcommittee Member
2020 **CSA** Innovations EPD Subcommittee Member, Annual Meeting Oversight Committee Member
2020- **SOAP** Intersociety Steering Committee Member

2020- **CSA** Pain Medicine Committee and Professional and Public Communication Committee Member
 2020- Stanford Anesthesia Department Mentorship Program (**AMP**): Mentor/Sponsor
 2020 **WHO** Technical Advisor: WHO Recommendations for Prevention and Treatment of PPH
 2020- **ACOG** Voluntary Review of Quality of Care program reviewer
 2019- **SOAP** International Outreach Committee
 2019 **WHO** Technical Consultation: Treatment of pre-eclampsia and eclampsia
 2018- **ASA** Committee on Obstetric Anesthesia
 2018 **WHO** External Review Group: WHO recommendations for Uterotonics for the prevention of PPH
 2017-18 **SOAP** President
 2017- **SOAP** Centers of Excellence: Founder and Chair
 2016 1st **World Congress of Anesthesia for Obstetrics** Planning Committee
 2016 **CMQCC** (California Maternal Quality Care Collaborative) Task Force: Advisory Group
 2014- **CSA** Educational Programs Division Committee
 2013- **ASA** Obstetric Anesthesia Educational Subcommittee
 2013 **AHA** (American Heart Association) Cardiac Arrest in Pregnancy Scientific Statement Writing Group
 2012-20 **CSA** District 4 Delegate
 2011-19 **SOAP Sol Shnider** Annual Meeting Planning Committee
 2011-21 **International Journal of Obstetric Anesthesia** Editorial Board Member
 2009-10 **ASA** Obstetric Anesthesia Research Subcommittee
 2008-14 **Faculty of 1000** Medicine, Evaluation Board Faculty Member,
 2007-20 **SOAP** Research Committee Member
 2006 **IARS** (International Anesthesia Research Society) Mentorship Initiative Mentor
 2005 **FAER** (Foundation for Anesthesia Education & Research) Medical Student Research Fellow Mentor

Academic and Professional Honors (Selected):

SOAP Best Paper of Annual Scientific Meeting: 2021 Finalist (Senior Author); 2021 Finalist (Co-Author); 2020 2nd place Best Clinical Study (Senior Author); 2020 Finalist Best Basic Science (Co-Author); 2018 Finalist (Co-Author); 2017 2nd place (Senior Author); 2016 1st place (First Author); 2015 Finalist (First Author); 2014 1st place (First author); 2012 1st place (First Author); 2011 Finalist (Senior Author); 2010 Finalist (First Author).
SOAP Gertie Marx Symposium Best Mentored Research: 2021 Winner (Co-Author); 2020 Winner (Co-Investigator); 2019 Finalist (Senior Author); 2017 Finalist (Co-Author); 2016 Finalist (Co-Author); 2015 2nd place (Senior Author); 2014 1st place (Senior Author); 2012 3rd place (Co-Author); 2009 2nd place (Senior Author); 2007 3rd place (Senior Author); 2006 1st place (Senior Author); 2004 2nd place (Co-Author); 2003 3rd place (First Author).
SOAP Zuspan Best Collaborative Research: 2019 3rd place (Senior Author); 2016 1st place (First Author)
Ellis N. Cohen Lifetime Achievement Award 2021, Department of Anesthesiology, Stanford
SOAP 2021 Teacher of the Year >10 years
Obstetric Anaesthetists Association of Great Britain: 2018 Best Paper Finalist (Co-Author); 2016 Best Poster Category (Co-Author); 2014 Best Paper Finalist (First Author); 2006 Best Abstract (Senior Author).
ASA 2017 Best Clinical Paper of Scientific Meeting Presentation (Co-Author)
 Stanford University Anesthesiology Department: 2014 and 2015 Best Clinical Abstract (Co-Author)
Canadian Anesthesiologists' Society: 2012 Best Paper in Obstetric Anesthesia Award (Senior Author)
SOAP 2012 Teacher of the Year <10 years
 Stanford University Teaching Scholar Award 2012
Attending of the Year Award 2006: Stanford University Anesthesiology Department
 SPCTRM Intensive Clinical Research Course, Stanford University: 2006 Best Protocol
 Stanford University Anesthesiology Department: 2003 and 2007 Attending of the Month Award

C. Contributions to Science

1. Peripartum device, drug and monitoring development

Our research has helped develop devices to improve labor epidural analgesia, objectively monitor labor pain, and optimize devices for monitoring after childbirth. We have developed patient-centered strategies to optimize pain management and reduce opioid use after cesarean delivery. The novel shared decision making postpartum pain management strategies we introduced allows personalized pain management, and directs analgesic medication to those who most need it. My research was recognized by the SOAP at several best research of the meeting symposiums.

- a. Riley ET, **Carvalho B**. The Episure syringe: a novel loss of resistance syringe for locating the epidural space. *Anesth Analg*. 2007;105(4):1164-6. PMID: 17898406
- b. Eisenried A, Austin N, Cobb B, Akhbardeh A, **Carvalho B**, Yeomans DC, Tzabazis AZ. Correlation of changes in hemodynamic response as measured by cerebral optical spectrometry with subjective pain ratings in volunteers and patients: *J Pain Res*. 2018;11:1991-1998. PMID: 30288094.
- c. Weiniger CF, Akdagli S, Turvall E, Deutsch L, **Carvalho B**. Prospective Observational Investigation of Capnography and Pulse Oximetry Monitoring After Cesarean Delivery With Intrathecal Morphine. *Anesth Analg*. 2019;128(3):513-522. PMID: 29958217
- d. **Carvalho B**, Mirza F, Flood P. Patient choice compared with no choice of intrathecal morphine dose for caesarean analgesia: a randomized clinical trial. *Br J Anaesth*. 2017;118(5):762-771. PMID: 28486595
- e. **Carvalho B**, Sutton CD, Kowalczyk J, Flood PD. Efficacy of Patient Choice of Different Postoperative Analgesic Protocols After Cesarean Delivery: A Randomized Prospective Clinical Trial. *Reg Anesth Pain Med*. 2019;44(5):578-585. PMID: 30867278

2. Pharmacokinetics and pharmacodynamics of peripartum medications

Many drugs are extensively utilized in expectant women, but these drugs have not been studied in the pregnant population. Due to physiological changes in pregnancy that may affect drug handling, there is a critical need to adequately study the pharmacokinetics and pharmacodynamics of drugs given to pregnant women and exposed fetuses. I have completed several pharmacokinetics and pharmacodynamics studies of drugs administered to pregnant women including epidural morphine, cefazolin, ondansetron, fentanyl, ampicillin, gentamycin, and magnesium. These research projects have produced valuable data to better appreciate pharmacokinetics and pharmacodynamics differences of drugs in pregnant women compared to non-pregnant women, and understand placental transfer and neonatal pharmacokinetic parameters. The WHO used data from our studies to develop optimal magnesium dosing strategies to treat pre-eclampsia. Our research will facilitate optimal maternal and fetal dosing protocols based on pharmacokinetics and pharmacodynamics mathematical modeling. Individualized dosing algorithms will significantly reduce maternal and neonatal side effects while maintaining therapeutic efficacy. The research was recognized by SOAP and selected for best research study presentations.

- a. Elkomy MH, Sultan, P, Drover DR, Ekaterina E, Galinkin JL, **Carvalho B**. Pharmacokinetics of Prophylactic Cefazolin in Parturients undergoing Cesarean Delivery. *Antimicrob Agents Chemother*. 2014;58(6):3504-13. PMID: 24733461
- b. Brookfield KF, Su F, Drover DR, Elkomy MH, Adelus M, Lyell DJ, **Carvalho B**. Pharmacokinetics and Placental Transfer of Magnesium Sulfate in Pregnant Women. *Am J Obstet Gynecol*. 2016;214(6):737.e1-9. PMID: 26767791
- c. Brookfield KF, Elkomy M, Su F, Drover DR, **Carvalho B**. Optimization of Maternal Magnesium Sulfate Administration for Fetal Neuroprotection: Application of a Prospectively Constructed Pharmacokinetic Model to the BEAM Cohort. *J Clin Pharmacol*. 2017;57(11):1419-1424. PMID: 28589614
- d. Brookfield KF, Tuel K, Rincon M, Vinson A, Caughey AB, **Carvalho B**. A randomized trial of an alternate dosing protocol for magnesium sulfate in obese preeclamptic women *Obstet Gynecol*. 2020;136(6):1190-1194. PMID: 33156201
- e. Brookfield K, Galadanci H, Lihong D, Wenning L, Mohammed I, Suleiman M, Oladapo O, Witjes H, **Carvalho B**. Magnesium sulfate pharmacokinetics after intramuscular dosing in patients with preeclampsia. *AJOG Global Reports* 2021;1:100018

3. Enhanced recovery after childbirth

My research has focused on measuring and enhancing recovery after childbirth. We have developed an in-hospital patient-reported outcome tool to evaluate recovery after vaginal and cesarean delivery. This recovery measurement tool has been validated in a series of studies, translated into several languages, adopted for research and clinical practice throughout the world, and recommended as a core outcome measure to assess recovery after cesarean delivery. We have comprehensively determined key domains and elements of out-patient postpartum recovery, and produced systemic reviews to determine the best performing patient-reported outcome measures (PROMs) to guide clinical care and future research efforts. Our work provided key elements for the development of the SOAP consensus recommendations for Enhanced Recovery after Cesarean Delivery. We also recently developed a core outcome set for researchers and clinicians to use to measure recovery after cesarean delivery.

- a. Sultan P, Sadana N, Sharawi N, Blake L, El-Boghdadly K, Falvo A, Ciechanowicz S, Athar W, Shah R, Guo N, Jensen S, El-Sayed Y, Cella D, **Carvalho B**. Patient reported outcome measures assessing recovery after childbirth: A scoping and systematic review *JAMA Netw Open*. 2020;3(5):e205540. PMID: 32442292
- b. Sultan P, Ando K, Sultan E, Hawkins J, Chitneni A, Sharawi N, Sadana N, Blake L, Singh PM, Flood P, **Carvalho B**. A systematic review of patient-reported outcome measures to assess postpartum pain using Consensus Based Standards for the Selection of Health Measurement Instruments (COSMIN) guidelines. *Br J Anaesth*. 2021;127(2):264-274. PMID: 34016441
- c. Bollag L, Lim G, Sultan P, Habib AS, Zakowski M, Tiouririne M, Bhambhani S, **Carvalho B**. Society for Obstetric Anesthesia and Perinatology Consensus Statement on Enhanced Recovery After Cesarean Delivery *Anesth Analg* 2021;132(5):1362-1377. PMID: 33177330
- d. Sultan P, Sharawi N, Blake L, Ando K, Sultan E, Aghaeepour, **Carvalho B**, Sadana N. Use of Patient-Reported Outcome Measures to Assess Outpatient Postpartum Recovery: A Systematic Review *JAMA Netw Open*. 2021;4(5):e2111600. PMID: 34042993
- e. Sultan P, Jensen SE, Taylor J, El-Sayed Y, Carmichael S, Cella D, Angst MS, Gaudilliere B, Lyell DJ, **Carvalho B**. Proposed domains for postpartum recovery: A concept elicitation study *BJOG* 2022;129(1):9-20. PMID: 34536324

4. Persistent pain and opioid use after cesarean delivery

Cesarean delivery is associated with significant postoperative pain, and severe and persistent incisional pain and opioid requirements after delivery can profoundly impact maternal and neonatal health. I developed and validated a technique to collect and assay wound exudate from the surgical site to profile biochemical mediator response. This discovery has helped scientists better understand the role of cytokines in incisional pain and wound healing postoperatively, and has facilitated the study of systemic and peripherally-administered opioid-sparing analgesics. Our study data has provided evidence that wound instillation with a sub-therapeutic systemic dose of a non-steroidal anti-inflammatory is an effective anti-inflammatory and opioid-sparing strategy. The series of studies provide a solid rationale for peripheral versus systemic administration of analgesics, as well as provide mechanistic evidence of the biological consequences of modulating local inflammatory events in surgical wounds. This research has been recognized by SOAP with the best research study of the meeting award, and Faculty of 1000 has highlighted the impact of these studies to the sub-specialty of obstetric anesthesia.

- a. **Carvalho B**, Clark JD, Angst MS. Incisional Wound and Systemic Cytokines, Nerve Growth Factor, Prostaglandin E2 and Substance P Release Following Cesarean Delivery. *J Pain*. 2008;9:650-7. PMID: 18394968
- b. **Carvalho B** Clark JD, Qiao Y, Yeomans DC, Angst MS. The Effect of Continuous Wound Infiltration with Bupivacaine on the Local Release of Nociceptive and Inflammatory Mediators Following Cesarean Delivery *Anesth Analg* 2010;111(6):1452-9. PMID: 20861424
- c. **Carvalho B**, Clark DJ, Yeomans D, Angst MS. Collecting and Measuring Wound Exudate Biochemical Mediators in Surgical Wounds. *J Vis Exp*. 2012;(68):50133 PMID: 23117346
- d. **Carvalho B**, Lemmens H, Ting V, Angst M. The Effects of Continuous Subcutaneous Instillation of Ketorolac and Hydromorphone on Wound Biochemistry in Surgical Wounds following Cesarean Delivery. *J Pain* 2013;14(1):48-56. PMID: 23218935

Google Scholar Metrics: Citations: 10743; h-index: 57; i10-index: 177

A complete list of my published work can be found at:

My Bibliography *US National Library of Medicine:*

<https://www.ncbi.nlm.nih.gov/myncbi/1LCY82v888j/bibliography/public/>