

CODA APPENDICITIS TRIAL BRINGS TOGETHER PAST AND CURRENT DOS MEMBERS

A collaboration of past and current Department of Surgery members lead national trial to answer the question: Are antibiotics as good as surgery to treat appendicitis?

Antibiotics may be a good choice for some, but not all, patients with appendicitis, according to results from the Comparing Outcomes of antibiotic Drugs and Appendectomy (CODA) Trial, published in the [New England Journal of Medicine](#) on October 5, 2020. The CODA Trial was led by current Department of Surgery faculty members – Drs. [David Flum](#), Professor and Associate Chair for research served as Co-Principal Investigator, and [Giana Davidson](#), Associate Professor, directed the Clinical Coordinating Center, leading the participation of 25 clinical sites in 14 states across the US. Current faculty members [Joseph Cuschieri](#), Professor, and former faculty member Dr. [Heather Evans](#) led Harborview Medical Center’s participation in the trial. Affiliate Associate Professor, Dr. [Danielle Lavallee](#), led the CODA Stakeholder Coordinating Center.



Flum



Davidson



Cuschieri



Lavallee

Deciding Between Antibiotics & Surgery for Appendicitis: Findings from the CODA Study

First results of the CODA Study tell us that both antibiotics and surgery may be good options for treating appendicitis. Each treatment has pros and cons. If you have appendicitis, you can talk with your doctor about what is most important to you when deciding on your treatment.

	Antibiotics	vs	Surgery
Good Health	After 1 month, participants rated their general health about the same in both groups.		After 1 month, participants rated their general health about the same in both groups.
Initial Time in ER & Hospital	During the first visit, time spent in the ER or hospital was about the same in both groups.		During the first visit, time spent in the ER or hospital was about the same in both groups.
Symptoms Go Away	After 1 month, symptoms like pain or fever were about the same in both groups.		After 1 month, symptoms like pain or fever were about the same in both groups.
No Surgery	✓ About 7 in 10 (71%) did not have surgery within 3 months.		✗ An appendectomy is surgery.
No Initial Hospital Stay	✓ About half (47%) did not have to be admitted to the hospital for their antibiotics treatment.		✗ Almost all (95%) participants were admitted to the hospital for their surgery.
Less Work Missed	✓ Participants missed an average of 5.3 days of work.		✗ Participants missed an average of 8.7 days of school or work.
Fewer Healthcare Visits	✗ 9 in 100 (9%) participants needed to visit an emergency room or urgent care clinic within 3 months.		✓ 4 in 100 (4%) participants needed to visit an emergency room or urgent care clinic within 3 months.
Appendicitis Does Not Return	✗ Appendicitis can come back if the appendix is not removed. Future CODA reports will tell us how often that happens.		✓ The appendix is fully removed when surgery is successful.
One Time Treatment	✗ About 3 in 10 (29%) overall had surgery within 3 months. About 4 in 10 (41%) who had an appendix stone (appendicolith) had surgery within 3 months.		✓ Most likely to be completed in one hospital visit.
Complications (Unexpected Problems)	For every 100 participants, there were about 8 problems in the antibiotics group. There were about 4 problems for every 100 participants in the surgery group. The higher number of complications in the antibiotics group was related to participants who had a small stone in their appendix, called an appendicolith.		

The CODA Collaborative. A Randomized Trial Comparing Antibiotics with Appendectomy for Appendicitis. Published online October 5, 2020 at [NEJM.org](#).

For more information: [CODAStudy.org](#)

The CODA Trial is the largest study to date comparing appendectomy and antibiotics for appendicitis, with 1,552 participants enrolled (roughly three times larger than the previous largest trial) in the randomized cohort. Funded by the Patient-Centered Outcome Research Institute and designed in partnership with patient stakeholders, CODA aimed to answer the question, “Based on my unique characteristics, preferences, and outcomes of interest, are antibiotics as good as appendectomy?”

As the CODA Trial was ramping up, the team reached out to several Department of Surgery alumni to bring their own health systems on board. “We were striving for a trial that captured the range of severity of appendicitis cases, diversity of health systems, and the broad range of experiences in healthcare to better understand what ‘success’ in treatment looks like for our patients,” said Dr. Davidson. “Developing and successfully completing a trial that was able to recruit patients to randomize to surgery or medical therapy 24/7 at 25 sites across the US took a tremendous amount of trust, communication, and collaboration across our individual teams. UW has produced phenomenal surgeon leaders and researchers, and for many of us, the years of experience we had in training together was a catalyst to launch this work. I’m hopeful it will be the first of our work together.”

Five Department of Surgery alumni led the CODA trial at their hospitals: Dr. Damien Carter (Maine Medical Center); Dr. F. Thurston Drake (Boston Medical Center); Dr. Kate Mandell (Swedish Medical Center); Dr. Sabrina Sanchez (Boston Medical Center); and Dr. Callie Thompson (Vanderbilt University).

“For me, and I know for my partner Dr. Sanchez as well, the opportunity to lead a trial of this magnitude was a huge opportunity,” said Dr. Drake. “The pragmatic nature of the trial made it fit well in different clinical environments, and the CODA team, in particular Dr. Davidson and [CODA project manager] Erin Fannon, were really hands on in making sure we were successful.”

CODA results indicated that at least in the short-term, antibiotics are not worse than appendectomy for appendicitis, as measured by the EQ-5D13 measure of general health status. Among those assigned to antibiotics, there was an approximately 3 in 10 rate of appendectomy by 90 days, and patients with an appendicolith had a higher rate of appendectomy (25% if no appendicolith and 41% with appendicolith). Overall, antibiotics were associated with a higher rate of adverse outcomes than appendectomy, but this higher rate was largely driven by the appendicolith subgroup. Patients without an appendicolith were not at higher risk for complications. Antibiotics were associated with more days in both the emergency department and hospital after initial treatment. There were fewer days of missed work by both patients and caregivers in the antibiotics group. There is a chance of missing a cancer of

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CODA APPENDICITIS TRIAL BRINGS TOGETHER PAST AND CURRENT DOS MEMBERS (CONT.)

the appendix when an appendectomy is not done – CODA found cancers in 7/776 appendectomy-assigned and 2/776 antibiotics-assigned participants at 90 days with a mean age of 47 years (range 21 to 74). Clinical outcomes including the impact of a delay in diagnosis and risk factors associated with an occult neoplasm will be a future area of focus of the CODA trial to help patients and surgeons determine if an antibiotic or surgical treatment should be considered.

“There were advantages and disadvantages to each treatment, and patients will value these differently based on their unique characteristics, concerns, and perspectives,” said Dr. Flum. Some people will look at these trade-offs and find antibiotics an acceptable, or even preferable option. Others will look at these trade-offs and choose appendectomy. Clinicians, researchers, and health systems can play an important role in encouraging this individualized approach to treatment by developing and deploying decision support tools to help patients prioritize and weigh multiple outcomes.

The CODA Trial is ongoing and future publications will detail long-term results, factors associated with antibiotic treatment success, and results from observational and EMR-only cohorts.

CODA was managed by the team in the Department of Surgery’s [Surgical Outcomes Research Center \(SORCE\)](#). More information on the CODA Trial and results can be found on the [CODA website](#).



Dr. Sherene Shalhub

The [Aortic Dissection Collaborative](#), led by Dr. [Sherene Shalhub](#), Associate Professor, Division of Vascular Surgery, has received a funding award through the [Patient-Centered Outcomes Research Institute \(PCORI\)](#) Eugene Washington Engagement Awards program to convene a collaborative of patients with-and at risk for-aortic dissection.

The team aims to improve the management of aortic dissection and increase quality of life for people impacted by this condition. To do so, the collaborative is engaging stakeholders to build a research infrastructure focused on patient-centered outcomes. It will feature research training; support and networking among patients, physicians and researchers with expertise in aortic dissection; research consortia dedicated to aortic dissection; industry stakeholders; and patient advocacy groups.

The main deliverable over the next two years is to create a virtual research network and establish research priorities among the stakeholder group, Shalhub explained. These research priorities will then be used to guide future research proposals that reflect patient centered priorities.

Dr. Shalhub was recognized as a “Vascular Hero” through Vascular Cures’ #vascular-hero social media campaign. Each year, Vascular Cures honors, celebrates and appreciates heroes who are on the front line battling the devastating effects of vascular disease such as strokes, pulmonary embolisms, aortic aneurysms, vascular dementia and peripheral artery disease. Vascular Cures requested nominations by

posting the nominee’s photo or a story on social media (Twitter, Facebook, LinkedIn, Instagram) with the hashtag #vascular-hero and the tag @vascularcures.

Dr. Shalhub remarked, “I am deeply honored to be named a vascular hero: None of this work is possible alone and I am grateful for our partners in the VEDS and Aortic Dissection Collaboratives. Engaging patients as partners in the research process has been one of the most fulfilling experiences as a surgeon and researcher.”



Dr. Jonathan Sham

Dr. [Jonathan Sham](#), Assistant Professor, Division of General Surgery, published “[Management of primary hepatic malignancies during the COVID-19 pandemic: recommendations for risk mitigation from a multidisciplinary perspective](#)” in The Lancet Gastroenterology & Hepatology.

The management of hepatobiliary malignancies is complex and resource intensive. The COVID-19 pandemic imposed unique limitations on healthcare resources and access to care. Dr. Sham worked with an international team of experts to develop guidelines for the management of complex hepatobiliary malignancies during the pandemic to aid clinicians around the world in making difficult treatment decisions in real time.

Dr. Sham won Swim Across America’s Young Investigator Award for his research with Dr. Buddy Ratner Professor & Director, Department of Bioengineering, University of Washington, to develop a novel biopolymer that can be used during pancreatic surgery to reduce the rates of pancreatic fistula. [Vimeo video >>](#)

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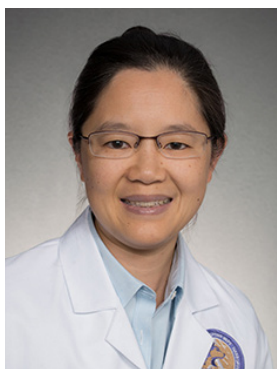


Dr. Barclay Stewart

Dr. **Barclay Stewart**, Assistant Professor, Division of Trauma, Burn & Critical Care Surgery, was awarded the Inaugural HMC Pilot Award to develop a new, innovative inter-disciplinary research collaboration and study the gut and wound microbiomes of patients with major burn injuries. The collaboration includes researchers from UW Medicine Regional Burn Center and collaborators from the UW Center for Microbiome Science and Therapeutics and the Salipante Lab. Their project aims to: describe shifts in the relative composition and function of gut and burn wound communities over the course of injury; and characterize strain-level communication between the gut and burn wound microbiomes. The findings will allow them to establish a novel interdisciplinary collaboration to study a new frontier in burn research: the role of the human microbiome in recovery from major injury. Additionally, Dr. Stewart and colleagues from Stanford University, Nepal Cleft and Burn Center and the Walter Reed laboratory in Nepal will be conducting a sister study that will allow comparison of the findings between two different environments and burn-injured populations. This line of investigation will inform interventions that positively influence the gut and wound microbiomes to improve survival and function after major burn injury.

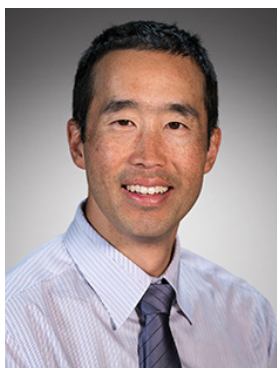
Dr. Stewart explains, "Together, this collaboration will allow us to develop interventions that may translate to improvements in resuscitation strategies that maintain gut mucosal health and immune function (e.g., enteral resuscitation), infection prevention and avoidance of multisystem organ dysfunction, novel approaches to wound healing (e.g., therapeutic microbial dressings), and prevention of pathologic hypertrophic scarring."

UW Medicine Regional Burn Center continues to support and conduct impactful research that transforms our understanding of patients' responses to injury and ways we might improve their outcomes.



Dr. Gale Tang

Dr. **Gale Tang**, Associate Professor, Division of Vascular Surgery, was appointed the new Associate Editor of JVS Vascular Science.



Dr. Raymond Tse

Dr. **Raymond Tse**, Associate Professor, Division of Plastic Surgery, was awarded the **American Association of Plastic Surgery's (AAPS)** 2020 James Barrett Brown Award. This award was established in memory of Dr. James Barrett Brown, past AAPS president, and is presented for the best plastic surgery paper published during the previous calendar year. The 2020 award recognizes Dr. Tse's paper "**Unilateral Cleft Lip Nasal Deformity: Foundation-Based Approach to Primary Rhinoplasty.**" Drs. **Craig Birgfeld**, Associate Professor, Division of Plastic Surgery, **Joseph Gruss**, Professor Emeritus, **Richard Hopper**, Maryls C. Larson, Professor of Craniofacial Surgery & Chief of Pediatric Plastic Surgery, Division of Plastic Surgery, and **Ezgi Mercan**, Craniofacial Image Analysis Researcher, Division of Plastic and

Craniofacial Surgery, Craniofacial Center, Seattle Children's Hospital, played significant roles in this research project as well. AAPS will present the award and \$2,000 prize to Dr. Tse at the AAPS Annual Meeting in May 2021.

Raymond Tse remarks, "In many ways, it's a special paper for us given that it challenges dogma and was Joe Gruss' last paper before he retired." As Rich Hopper noted, "Joe taught us all so much about how to address the cleft nasal deformity, and the paper was a great testimony to the fundamental concepts he brought to our team and specialty."



Dr. Nicholas Vedder

Dr. **Nicholas Vedder**, Professor of Surgery & Orthopaedics, Jamie Hunter Endowed Chair, Chief of Plastic Surgery, and Vice Chair, Department of Surgery, remarked, "Dr. Gruss also won this award in 1985 for a paper that again challenged dogma, describing his novel approaches to craniofacial trauma with primary bone grafting, something quite controversial at the time, but as we all know, has become the standard of care. We are all tremendously proud of our world-leading team of craniofacial surgeons who are our colleagues at the University of Washington."

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honors, awards & publications (cont.)



Dr. Eugene Zierler

Dr. **Eugene Zierler**, Professor, Division of Vascular Surgery, received the Society for Vascular Medicine's (SVM) 2020 Jess R. Young Outstanding Vascular Medicine Educator Award. This award is conferred upon individuals who have made an exemplary contribution to the field of vascular medicine through the education of its practitioners. The award is presented in honor of Dr. Jess R. Young, the first SVM president and Chairman of the Department of Vascular Medicine at the Cleveland Clinic, in recognition of his ground-breaking

work in the field of vascular medicine, his pre-eminence as an educator and his vision for multi-specialty programs.

"It was a very special honor to receive this award from the SVM. It is especially meaningful because it comes from a Society which is outside my primary specialty of vascular surgery," said Dr. Zierler. "The list of previous recipients includes some of the most respected names in vascular medicine, but only one other surgeon. I am grateful to the SVM leadership for this recognition."

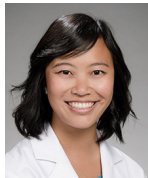
RESIDENTS



Beni



Dasari



Haruta

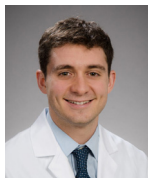


Miranda

Drs. **Catherine Beni**, Research Resident, **Mohini Dasari**, (R4) **Alison Haruta**, (R4) and **David Miranda**, (R4), **Joshua Rosen**, Research Resident, were nominated for the Harborview Medical Center "Outstanding Consultant of the Year Award" for the 2019-20 academic year by the University of Washington Department of Emergency Medicine Residency Program.



Little



Czerwonko-Pupi

Drs. **Christopher Little**, (R2) and **Matias Czerwonko-Pupi**, (R3), were nominated for the University of Washington Medical Center "Outstanding Consultant of the Year Award" for the 2019-20 academic year by the University of Washington Department of Emergency Medicine Residency Program.



Massenburg



Mehta

The Resident and Associate Society of the American College of Surgeons (RAS-ACS) selected Drs. **Ben Massenburg**, (R4), and **Kajal Mehta**, Research Resident, for two Global Surgery Work Group Leadership positions.

Dr. Massenburg will hold the Subspecialty Engagement Lead position and Dr. Mehta will be Secretary, which will advance to Vice Chair in 2021-22 then to Chair.

"I am excited to be working alongside Kajal and the other members of the ACS RAS Global Surgery Work Group as the Subspecialty Lead. With this group, I hope we can engage with other trainees, surgeons, and healthcare institutions to develop a bidirectional and multi-disciplinary partnership that will strengthen surgical health systems worldwide" said Dr. Massenburg. "I would like to thank Drs. **Jeffrey Friedrich**, Professor, Division of Plastic Surgery, **Kari Keys**, Associate Professor, Division of Division of Plastic Surgery, and **Richard Hopper**, Marlys C. Larson Professor of Craniofacial Surgery & Chief, Pediatric Plastic Surgery, Division of Plastic Surgery, for supporting my passion for global surgery during residency, and to Drs. John Meara and Nivaldo Alonso for their continued mentorship."

"I'm thrilled for the opportunity to work with Dr. Massenburg and other rising leaders in Global Surgery from around the country as Secretary of the RAS ACS Global Surgery Working Group." Dr. Mehta continues, "after our group's recent meeting, I am in awe of my colleagues' wide range of experiences and dedication - I am certain the coming years will be collaborative, productive and accelerate our progress in addressing surgical health inequity around the globe. I'd like to especially thank my mentor, Dr. **Barclay Stewart**, Assistant Professor, Division of Trauma, Burn & Critical Care Surgery, for his continual support, as well as Dr. **Douglas Wood**, The Henry N. Harkins Professor and Chair and Dr. **Karen Horvath**, Professor, Director, Residency Program in General Surgery, Associate Chair for Education, for their support of UW DOS Global Surgery initiatives."

"I have the fortune and opportunity to spend my first year of dedicated research time as an NIH Fogarty Global Health Research Fellow. This year is different due to the COVID-19 pandemic, but even then, I have had incredible opportunities in the past 2 months through the program. During our virtual NIH orientation (typically held at the NIH campus) in July, we worked on developing and practicing our "elevator pitch" for our research projects," said Dr. Mehta. "After giving my pitch to Dr. Roger Glass, the director of the Fogarty International Center, I was one of four fellows who had the opportunity to present my pitch "Enteral Resuscitation for Burn Injuries in Nepal" to Dr. Francis Collins, the Director of the NIH! This was an incredible honor in my early career that is built on the work and mentoring from generations of global surgery researchers at UW like Dr. **Barclay Stewart**, Assistant Professor, Division of Trauma, Burn & Critical Care Surgery and Dr. **Charlie Mock**, Professor, Division of Division of Trauma, Burn & Critical Care Surgery.

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Dr. **Catherine Beni**, a T32 Postdoctoral Research Fellow under the guidance of Dr. **Grant O'Keefe**, Professor, Division of Trauma, Burn & Critical Care Surgery, presented her work on improving the precision of IV fluid administration in trauma patients by utilizing mathematical modeling to create decision-making tools and feedback-control algorithms at the 2020 Pacific Northwest Sepsis Conference.

Intravenous (IV) fluids are a common treatment in the intensive care unit (ICU) to boost and maintain blood pressure or improve organ perfusion in patients suffering from shock. However, IV fluids are not entirely benign, and larger volumes of fluid are associated with complications including increased time on mechanical ventilation, risk of adult respiratory distress syndrome (ARDS), and need for continuous dialysis. Excess fluid is also a common problem: approximately one third of patients are discharged from the ICU with over 10% of their body weight in fluids. Knowing who will benefit from IV fluid and how much to give are major questions that remain unanswered. Further, there is controversy over whether these complications are a marker of illness severity – sicker patients tend to receive more fluid – or due to IV fluids themselves. Several randomized control trials have investigated restrictive versus liberal IV fluid strategies. While promising, these trials are also limited: half of the trials had no difference in given volume between the two strategies, and the other half were underpowered to show a significant difference in outcomes. Much work remains to be done on this important topic.

Restrictive vs Liberal: IVF use in septic shock

Meyhoff et al. 2020

Surviving Sepsis 2018

- Check lactate
- Blood cx before antibiotics
- Start broad-spectrum antibiotics
- **30 mL/kg crystalloid**
- Start vasopressors for unresponsive hypotension

1 hour bundle

Strong Recommendation, Low Quality of Evidence

"Although little literature includes controlled data to support this volume of fluid, recent interventional studies have described this as usual practice in the early stages of resuscitation, and observational evidence is supportive."

9 RCTs

Looking at restrictive vs conservative fluid strategies in sepsis

4 RCTs

Strategies differed in IVF volume

5 RCTs

Strategies did NOT differ in volume

Meta-analysis

No difference in any of:

- Mortality
- Vent-free days
- Pressor use
- ICU LOS
- RRT need/duration

But... total n: 415

grossly underpowered

Need n ≥ 2700 to detect 1 day difference in vent-free days, ICU LOS or 15% RR difference



@CatherineBeni

Pacific Northwest Sepsis Conference

2020

