Uniformed Services University

of the Health Sciences

"Learning to Care for Those in Harm's Way"

Board of Regents

Quarterly Meeting

May 17, 2024

BOARD OF REGENTS
UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES (USU)
220TH MEETING
May 17, 2024, 7:30 a.m. – 11:30 a.m. Eastern Time
Hosted in-person at the Board of Regents Room D-3001,
4301 Jones Bridge Rd, Bethesda, MD, 20814
and
Virtual by Google Meet

MEETING AGENDA

OPEN MEETING

7:30 – 7:35 a.m.:	**Meeting Call to Order**	
	Designated Federal Officer	Ms. Annette Askins-Roberts
	Opening Comments	
	Chair, Board of Regents, USU	Dr. Nancy Dickey
7:35 – 7:50 a.m.:	**Health Affairs Update**	
	Assistant Secretary of Defense (HA)	HON Lester Martínez-López
7:50 – 8:50 a.m.:	**President's Report and Discussion**	
	President, USU	HON Jonathan Woodson
8:50 – 9:10 a.m.:	**End of Academic Year Summary**	
	Dean, School of Medicine	Dr. Eric Elster
	Dean, Graduate School of Nursing	Dr. Carol Romano
	Dean, Postgraduate Dental College	Dr. Drew Fallis
	Interim Dean, College of Allied Health Sciences	Mr. Andrew Reimund
9:10 – 9:20 a.m.:	**Discussion**	
9:20 – 9:30 a.m.:	**Break**	
9:30 – 10:00 a.m.:	**SOM Admissions Process Update and Discussion**	
	SOM Assoc. Dean, Admissions & Recruitment	COL Danielle Holt
10:00 – 10:30 a.m.:	**USU Accreditation Policy and Middle States Commission on Higher Education Update and Discussion**	
	Assistant VP for Accreditation	Mr. Stephen Henske
	Dir., Accreditation Support Services	Mr. Brian Rimm
10:30 – 11:25 a.m.:	**National Disaster Medical System Pilot Program Brief and Discussion**	

	Director, National Center for Disaster Medicine and Public Health	Dr. Jeffrey Freeman
11:25 – 11:30 a.m.:	**Closing Comments**	
	Chair, Board of Regents, USU	Dr. Nancy Dickey
	Adjourn	
	Designated Federal Officer	Ms. Annette Askins-Roberts

BOARD OF REGENTS
UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
220th MEETING

May 17, 2024 7:30 a.m. - 2:30 p.m. Eastern Time

TABLE OF CONTENTS

Reports to the Board of Regents

TAB 1

Health Affairs Update

TAB 2

President's Report

TAB 3

End of Academic Year Summary

School of Medicine

School of Medicine
2023 – 2024 Academic Year in Review

Eric Elster, MD, FACS, FRCS Eng (Hon.)
CAPT, MC, USN (Ret.)
Professor of Surgery
Professor of Molecular and Cell Biology
Dean, School of Medicine

May 17, 2024

USU
Uniformed Services University

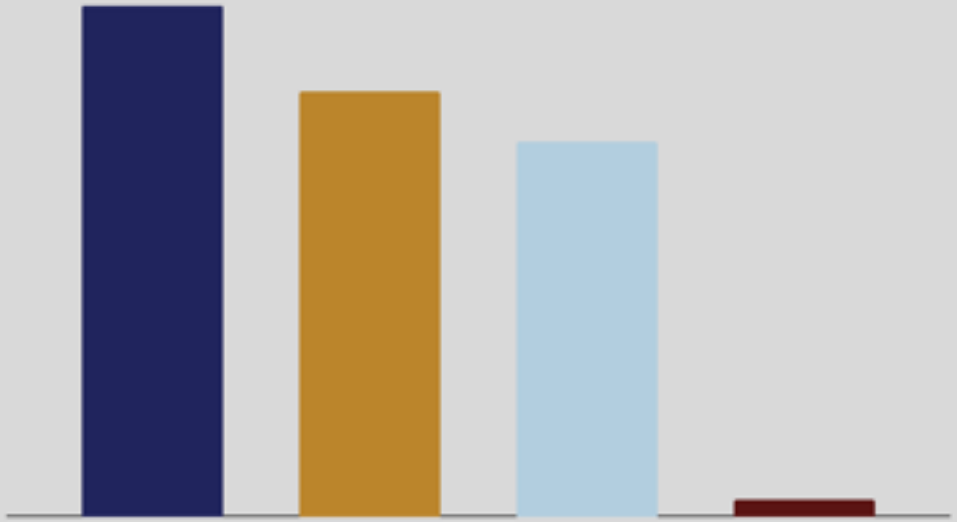
Academic Year 2023 - 2024

- Medical education (Class of 2024, AAMC and LCME update, Department of HPE, commitment to student success)
- Graduate education
- Awards and accomplishments (Faculty, medical students, graduate students)
- Research and innovation
- Advancing military medicine
- Leadership updates

Class of 2024

156 *MD graduates in the Class of 2024*

By Service Branch



Match Rate

86% match to specialty

Capstone Research

80% completed Capstone research projects

EMDP2

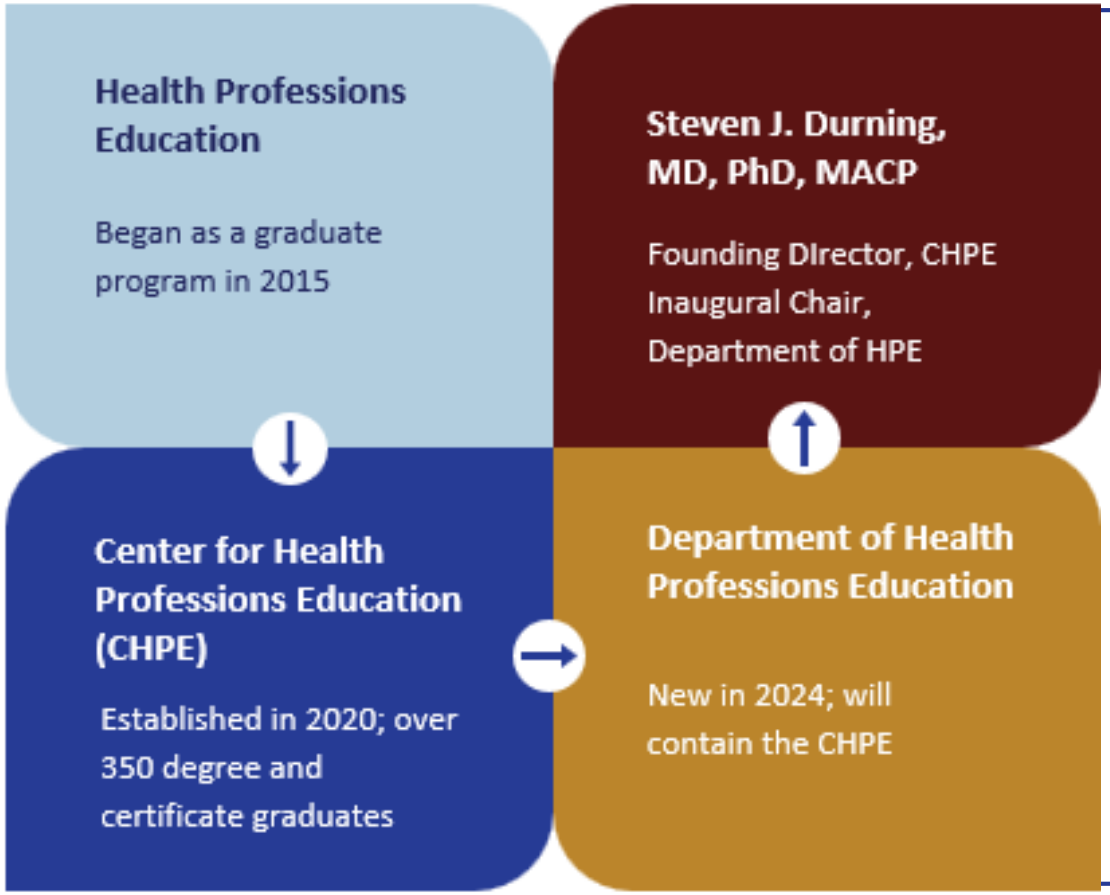
13 Enlisted to Medical Degree Preparatory Program graduates - 8.3%

MD / PhD

3 Physician - Scientist graduates

USU
Uniformed Services University

Welcoming the Department of Health Professions Education



Health Professions Education at USU

- **DEPARTMENT of HPE** - Focal point for educational research and innovation - responsible for the Distance Learning (DL) Lab and will co-lead development of the new Education and Simulation Hub
- **CHPE** - Will maintain its specialized focus on HPE research, especially the Long-Term Career Outcomes Study (LTCOS)
- Dedicated to education, leadership, scholarship, and service, the Department and Center will strengthen USU's position as a ***national and international leader in Health Professions Education***

USU
Uniformed Services University

LCME Accreditation Update and AAMC GQ Survey (Class of 2023)

Institutional Self-Study
COMPLETE ✓

Survey Visit
COMPLETE ✓

LCME Review
COMPLETE ✓

LCME Determination — **Summer 2024**

94.8%

AAMC Graduate Questionnaire (GQ):
"Overall, I am satisfied with the quality of my medical education"

94.8% of USU Class of 2023 medical students **Agree** or **Strongly Agree**, compared to 89.4% of all medical students nationally. *More USU students responded Agree or Strongly Agree than all students nationally in 2021, 2022, and 2023.*

Faculty and Resident Teaching

USU students gave higher scores across **ALL SPECIALTIES** than all students nationally.

Preparation for Residency

In 7 of 9 measures, a higher percentage of USU students reported feeling prepared for residency than all students nationally.

Faculty Professionalism

Reporting on 14 behaviors associated with professionalism, USU students "Very Often" or "Always" observed these behaviors in faculty at rates higher than all medical students nationally.

Quality of Clinical Clerkships

USU students gave equal or higher scores for quality of clerkship experience compared to all other medical students.

Basic Science Preparation

In 11 of 14 disciplines, more USU students reported satisfaction with their basic science education compared to all students nationally.

USU
Uniformed Services University

Commitment to Student Success

Longitudinal Coaching Program

Pairs students and faculty coaches who meet at regular intervals throughout medical school (12 sessions) - Class of 2026 students, the program's first participants, reported that having a coach:

- ➔ Enhanced their well-being
- ➔ Enabled them to better recognize and respond to feedback
- ➔ Provided accountability for their progress toward academic and personal goals

Assessment Dashboards

- ➔ Over 10 analytic dashboards provide real-time visualizations
- ➔ Visualizations deliver actionable insight that helps students and faculty to address performance gaps
- ➔ Effective use of assessment data facilitates longitudinal tracking, enhances faculty oversight and mentorship, and fosters a culture of excellence and accountability

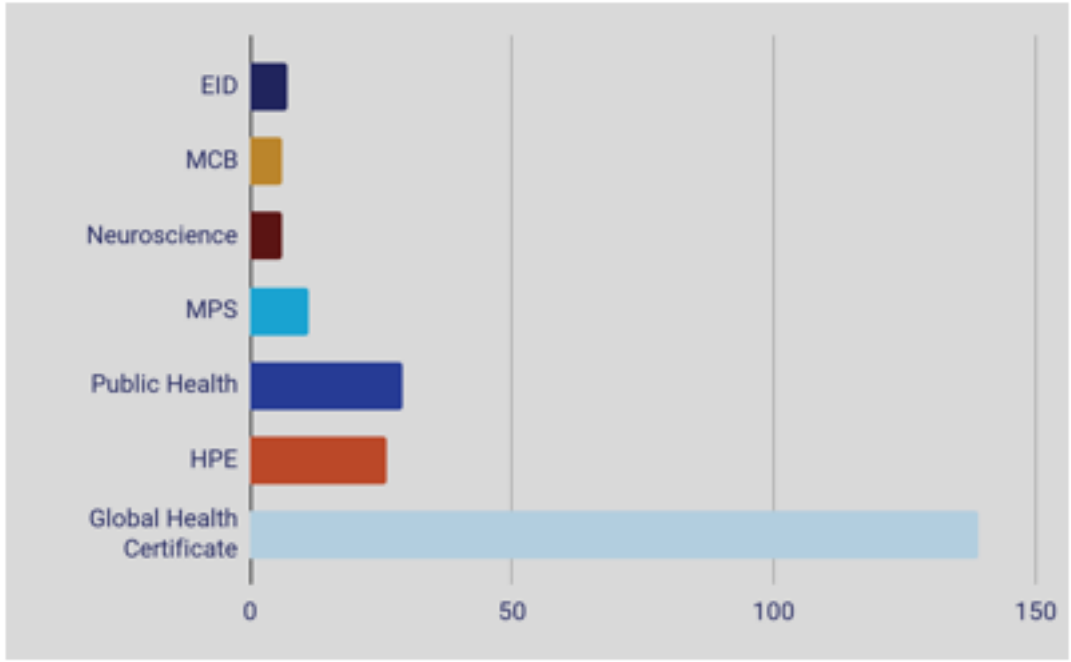
Graduate Education

Civilian v. Military

Military: 197 (includes 139 Global Health Certificate graduates)- 89%

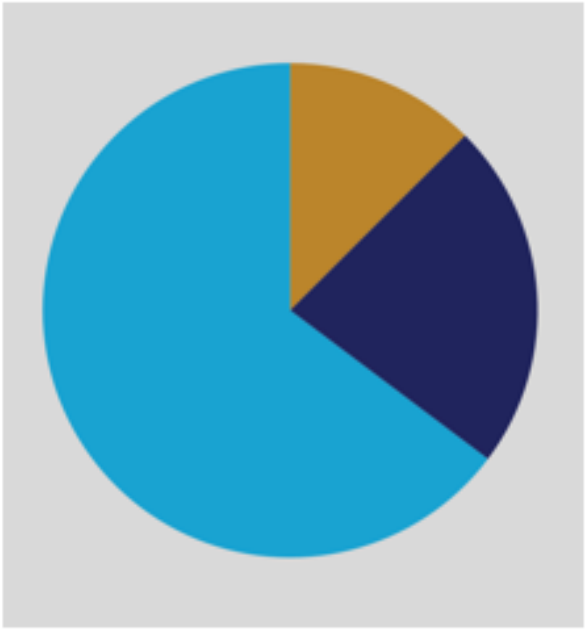
Civilian: 24 - 11%

Graduates (#) by Program



Emerging Infectious Diseases: 7
Molecular and Cell Biology: 6
Neuroscience: 6
Medical and Clinical Psychology: 11
Health Professions Education: 29
Global Health Certificate: 139

Degrees



Master's: 51 (23%)

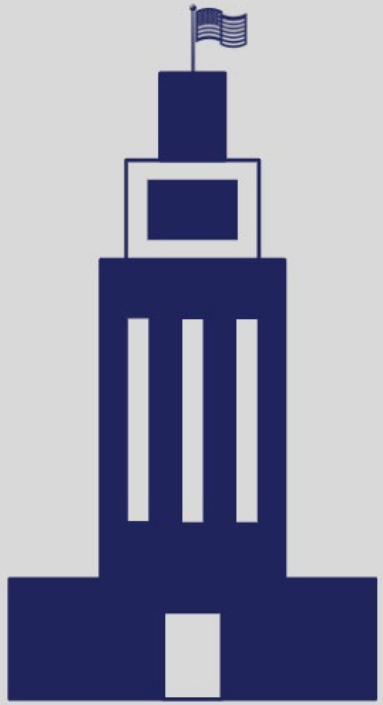
PhD: 28 (13%)

Certificates: 145 (65%)

USU
Uniformed Services University

Graduate Medical Education (GME) : the National Capital Consortium

About the NCC



- The largest GME footprint in the MHS
- NCC has Institutional Oversight and is organizationally within the School of Medicine
- Includes USU, WRNMMC, A.T. Augusta Military Medical Center, and Malcolm Grow Medial Clinics and Surgery Center
- All internship, residency, and fellowship programs are fully accredited

AY 2023 - 2024: By the numbers

62 62 internship, residency, fellowship and allied health programs

Only ***7*** citations across ALL programs (vs. typical 1 or 2 per program)

96.5%

NCC students achieved a ***96.5% first-time pass rate*** for Board certification exams

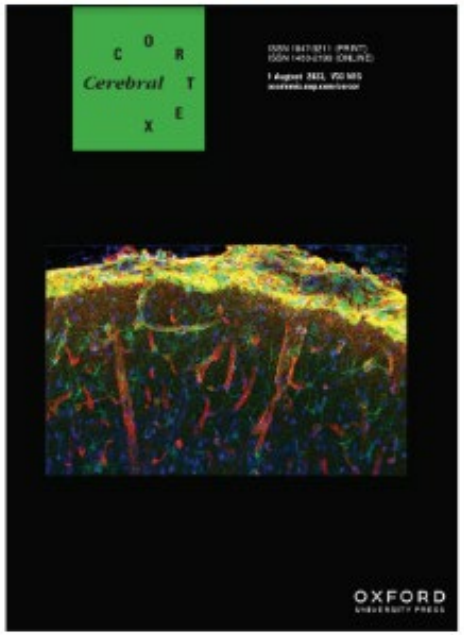
256 2024 graduates: 134 Army, 90 Navy, 26 Air Force, 2 PHS, 1 Canadian Air Force, 3 civilians

Selected Accomplishments - Medical Students

- **2LT Ha Kim, 2LT Sabreenah Khan, 2LT Emamake Odafe, 2LT Dave Holovac, and 2LT Rebecca Beard:** Developed and taught an ultrasound skills module
- **2LT Mason Remondelli 2LT Spencer Allen:** USMA "30 Under 30" Leader Developer Award)
- **ENS Alexius Russell:** EMDP2 student; appeared on the "WarDocs" podcast
- **2LT Brent Bubany**: Pat Tillman Scholarship
- **ENS Claire Sturek**: ACOG Gibbons Award

- **2d Lt Andy Bayne and 2d Lt Noah Smith:** U.S. Patent, "Multilayer Glove Loader"
- **2LT Michael Deegan and 2LT Gartrell Bowling:** Army Sapper tabs
- **ENS Megan McLaughlin**: Selected for Team USA, International Military Sports Council soccer tournament
- **ENS Mary "Katie" Robey:** Selected to represent Navy on the All-Navy Women's Basketball team
- **ENS Elizabeth Sullivan:** Second place, Armed Forces Cross Country Championship

Selected Accomplishments - Graduate Students



- **Major Simon Tallowin (MCB):** Senior Research Fellow, UK Academic Department of Military Surgery and Trauma
- **Megan Parker** (MPS): 2024 NIH Fellows Award for Research Excellence (FARE)
- **Laura Novak** (MPS): APA Division 19 Student Research Awards
- **Nicholas Breehl (NES):** Cover artist, August issue of *Cerebral Cortex*
- **ENS Britney Bessarab, ENS Charlcie Roman, ENS Norbert Owusu, CPT Chad Beach** (MHAP): First and second place at inaugural DMV Case Collaborative competition, George Mason University

Awards and Accomplishments - Faculty







- **Dr. Thomas Davis:** MHSRS Distinguished Service
- **Dr. Vincent Ho:** AHA CVRI Distinguished Achievement Award
- **Col Kerry Latham:** ACS Humanitarian Award
- **Dr. Kyle Potter:** COL Brian Allgood Memorial Leadership Award (SOMOS)
- **Col Trimble Spitzer:** ACOG Armed Forces District Mentor of the Year
- **CAPT Tamara Worlton:** Fulbright Alumni Ambassador
- **Drs. Paige Waterman and Naomi Aronson:** Masters, American College of Physicians




- **LTC Milissa Jones:** NMQF 40 Under 40 for Minority Health
- **Dr. Vijay Singh:** Honorary Professor, Amity University (India)
- **Col Pamela Williams:** AAMC Excellence in Medical Student Career Advising
- **Dr. Leonard Sperling:** American Society of Dermatopathology Helwig Award



- **Dr. Joshua Hartzell:** ACP Sol Katz Award
- **CPT Emily Parsons:** AAP Outstanding Young Pediatrician
- **Dr. Joseph Lopreiato:** AAP Halamek Award
- **Dean Eric Elster:** Distinguished Member of the Excelsior Surgical Society

Research and Innovation

AY 2023 - 2024: 93 awards ≥$500K

Infectious Disease ($20,804,748)
PAIVED, EPICC EID, COVIVA-1

Combat Casualty Care ($1,421,915)
Innovations in Combat and Burn Casualty Care
Next Gen Therapeutic Peptides

TBI ($2,152,422)
Role of the Endocannabinoid Selective COX-2 Inhibition in Post-Traumatic Headache Associated with Repetitive Mild Traumatic Brain Injury

Suicide Prevention ($856,832)
PTSD Training in Evidenced Based Treatments, PTSD Assessment, and Management of Suicide Risk, and Military Culture for Clinicians Treating Veterans

Pediatrics ($741,044)
Molecular Analysis of MEHMO Syndrome Mutations in Translation Factor EIF2

Women's Health ($1,806,208)
The Development of a Clinical Predictive Tool to Predict Osteoporosis and Fractures in Women using Serum Biomarkers

CBRN (>$9 million)
Includes NIAID and JPEO-CBRN grants to study radiation countermeasures

2023 (CY) Research Funding

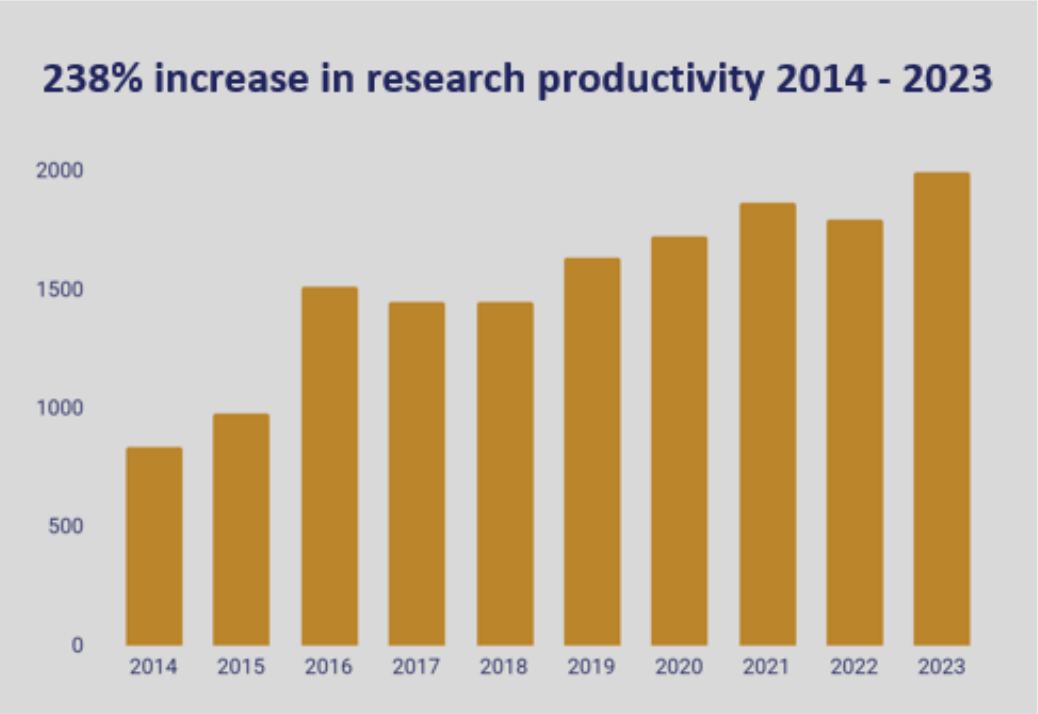
Over $401 million
Total research funding awarded

$62.8 million
Congressional funding

$163.3 million
Core funding

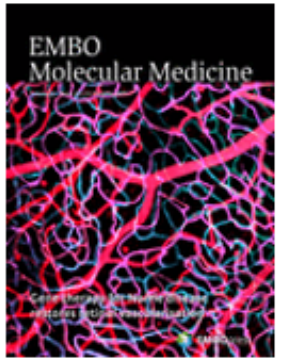
$175.1 million
Competitive (peer-reviewed) funding

Research and Innovation cont.



Newsworthy and Notable

- "mAb therapy controls CNS-resident lyssavirus infection via a CD4 T cell-dependent mechanism," (Mastraccio, Schaefer, Broder, Huaman)
- "Neuronal tau pathology worsens late-phase white matter degeneration after traumatic brain injury in transgenic mice" (Yu, Iacono, Perl, Lai, Gill, Le, Lee, Sukumar, Armstrong)
- "The influence of microbial colonization on inflammatory versus pro-healing trajectories in combat extremity wounds" (Schobel, Gann, Unselt, et al)
- "The Best PTSD Treatment You've Never Heard Of," (Garry Trudeau, Washington Post July 2023) – op-ed on PTSD research, Reconsolidation of Traumatic Memories (RTM) (Dr. Michael Roy)
- *Popular Science* Top 50 Innovations of 2023: 4D Bio 3's meniscus biofabrication technology, used aboard the International Space Station
- CHSR's A cohort study of BMI changes among U.S. Army soldiers during the COVID-19 Pandemic was widely cited in academic and popular media



The Washington Post

Democracy Dies in Darkness

Opinion | The best PTSD treatment you've never heard of

By Garry Trudeau

July 10, 2023 at 7:00 a.m. EDT

USU
Uniformed Services University

Advancing Military and Public Health at Home and Abroad

TBI	Health Disparities	Opioid Misuse	Suicide Prevention	Infectious Disease	Cancer	Gender-Based Violence	Trauma Surgery	International Engagement
								
CNRM becomes the Military Traumatic Brain Injury Institute (MTBI^2) reflecting its mission of research and care for TBI in the military - rebrand campaign wins 3 Silver ADDY Awards	Departments and Centers (GSO, MED, CHSR, SUR, PED) publish research aimed at identifying and addressing disparities in health care and health outcomes.	DVCIPM partners with DHA to increase naloxone Rx rates for patients with elevated opioid overdose risk; DHA compliance rate nearly 80 percent as a result	Understanding and addressing suicide risk in the military: MPS Suicide CPR Initiative; CDP, CMPH, and CSTS research studies	IDCRP contributes to updated JTS clinical practice guidelines for invasive fungal infections; also publishes research and provides consultation (FDA, White House OPPR) on COVID and Long COVID	MCCRP's newly acquired high performance data storage cluster enables proteogenomic and molecular data analysis supporting multiple Cancer Moonshot research projects	Dr. Lynn Lieberman Lawry (PMB) led multiple overseas engagements on GBV (Central America, South America, Zambia)	USU-developed CME courses (ASSET+, COTS+, CCTS) ensure combat readiness for surgeons and exceptional care in the field for warfighters	PSY, CDP, and CSTS (COL Vincent Capaldi, Dr. Curt West, Dr. William Brim, Dr. David Benedek) provided training and support for Ukrainian psychiatrists

Leadership Updates

Dr. Paige Waterman
Chair, Medicine

Dr. Steven Durning
Chair, new
Department of HPE

COL Danielle Holt
Associate Dean, Admissions and Recruitment

LTC Robert VIetor
Chair, Anesthesiology

Dr. Jamie Mancuso
Chair, Preventive Medicine and Biostatistics

COL Vincent Capaldi
Chair, Psychiatry

Lt. Col. David Lindholm
Associate Dean for Regional Education, San Antonio

LTC Bradley Dengler
Director, Military Traumatic Brain Injury Initiative (MTBI^2)

TAB 4

End of Academic Year Summary

Graduate School of Nursing

Uniformed Services University Daniel K. Inouye Graduate School of Nursing (GSN)

For Board of Regents May 2024

Carol A. Romano PhD, RN, FAAN Dean & Professor

Graduate Nursing
Uniformed Services University

National Recognition

1. US News & World Report 2025 Graduate Schools of Nursing
   - 651 Academic accredited Nursing Schools surveyed
   - Ranking based on 15 quality indicators
     (research, faculty credentials, recourses)

   GSN Doctor of Nursing Practice : # 26

   GSN Masters of Nursing Science: #76

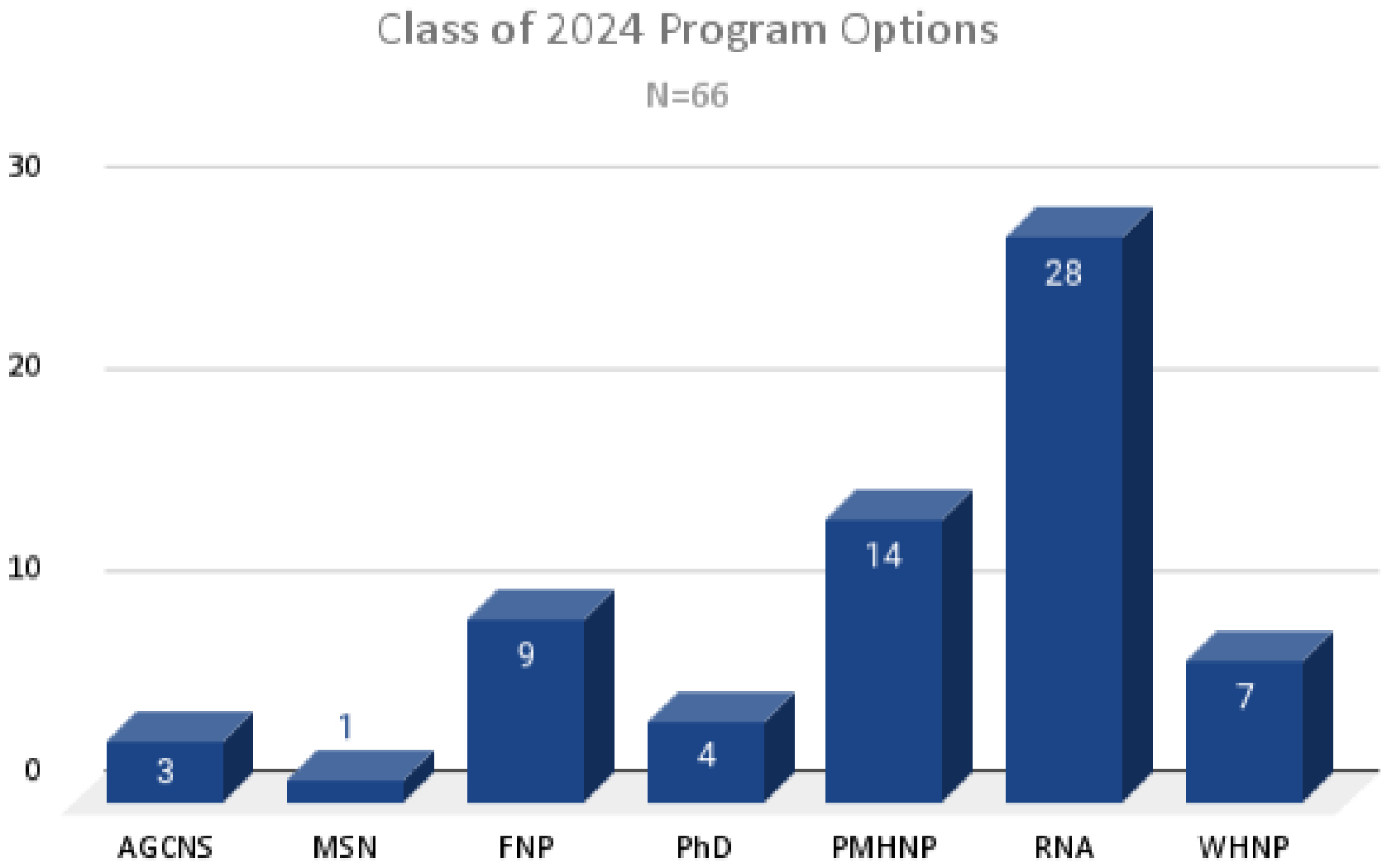
   GSN Nurse Anesthesia Program: #1

2. Two NLN Center of Excellence Designations:

Enhancement of Student Learning & Faculty Pedagogy

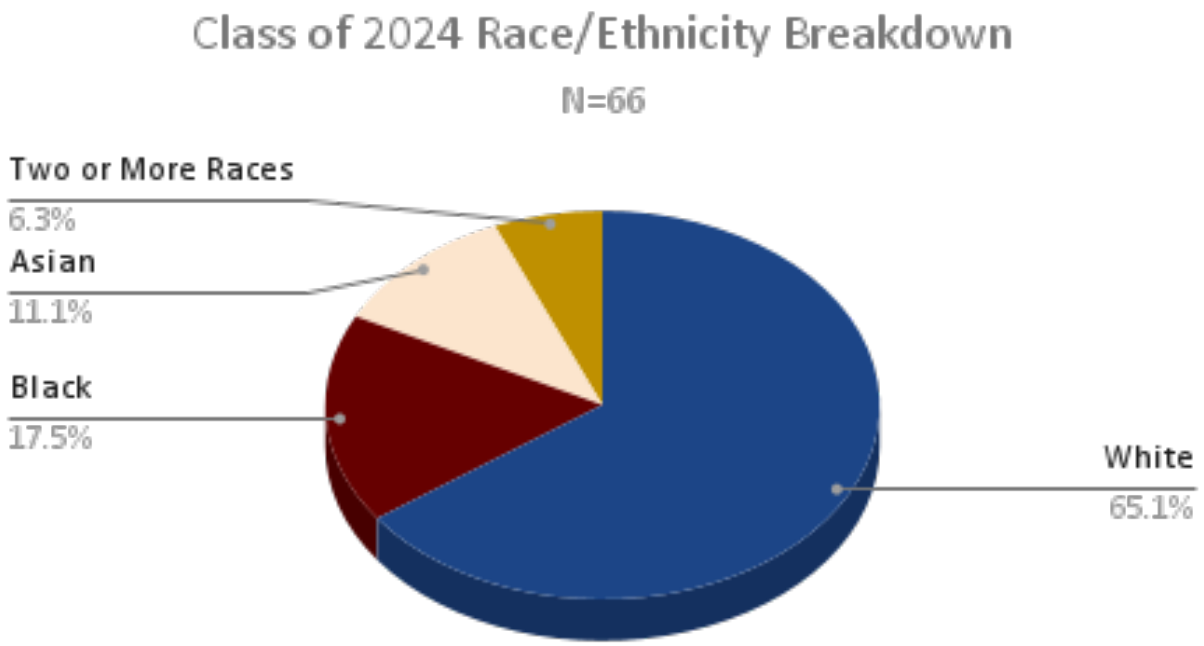
Graduate Nursing
Uniformed Services University

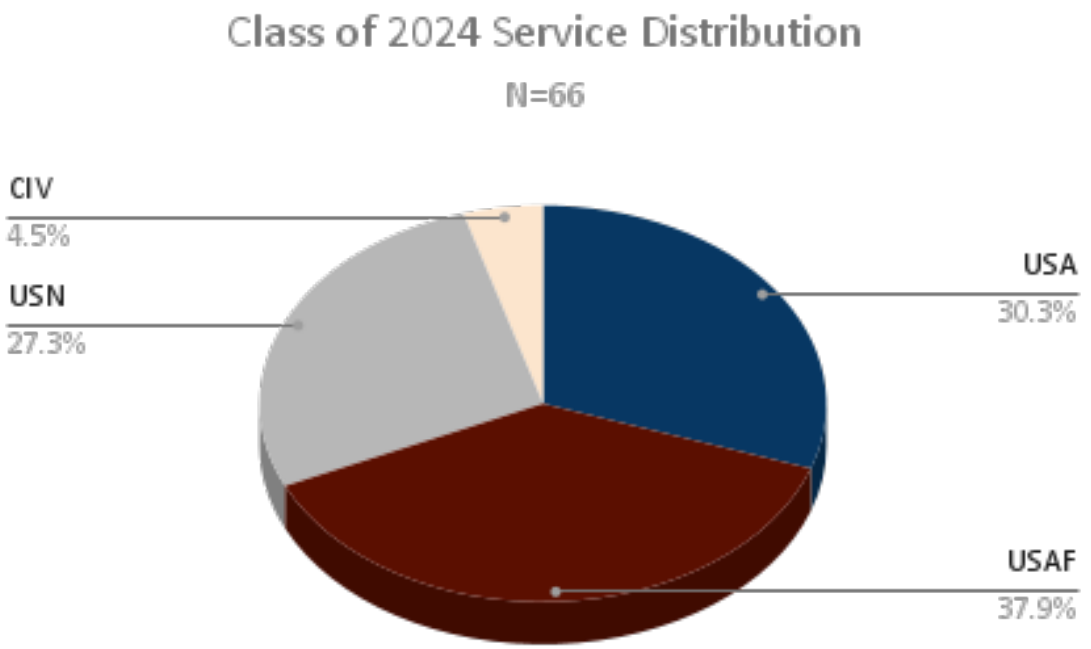
Graduating Students: Class of 2024



Graduate Nursing
Uniformed Services University

Graduating Students: Class of 2024





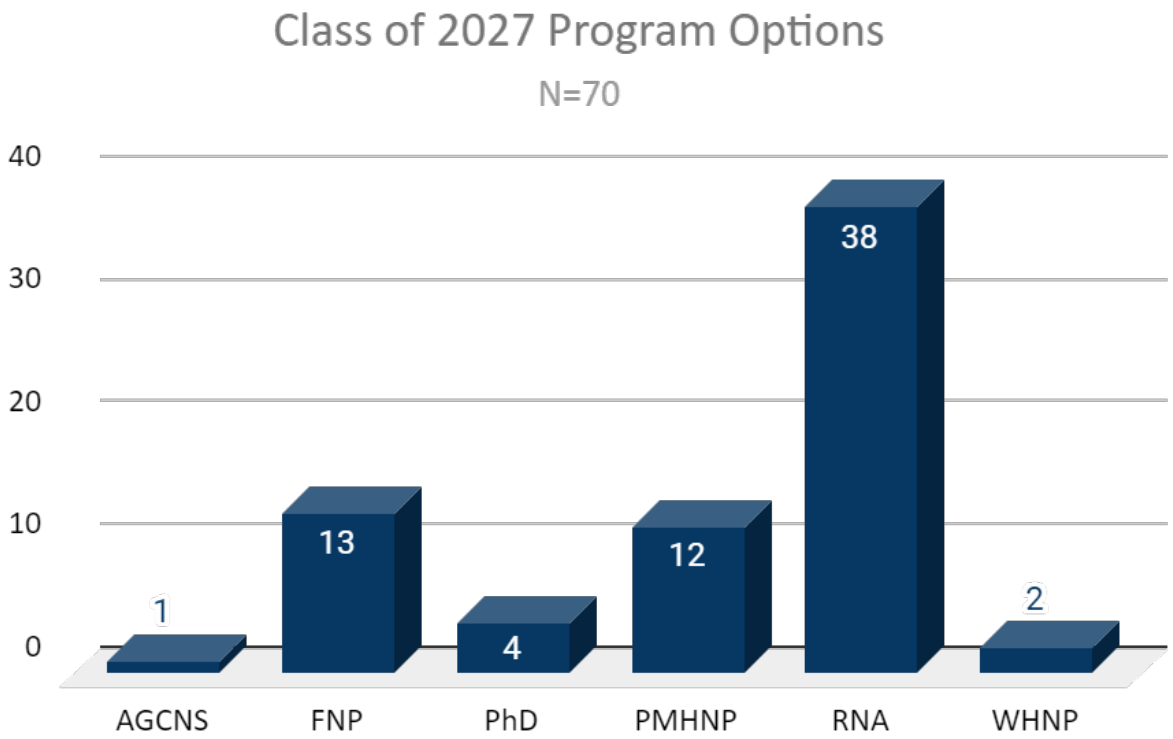
Graduate Nursing
Uniformed Services University

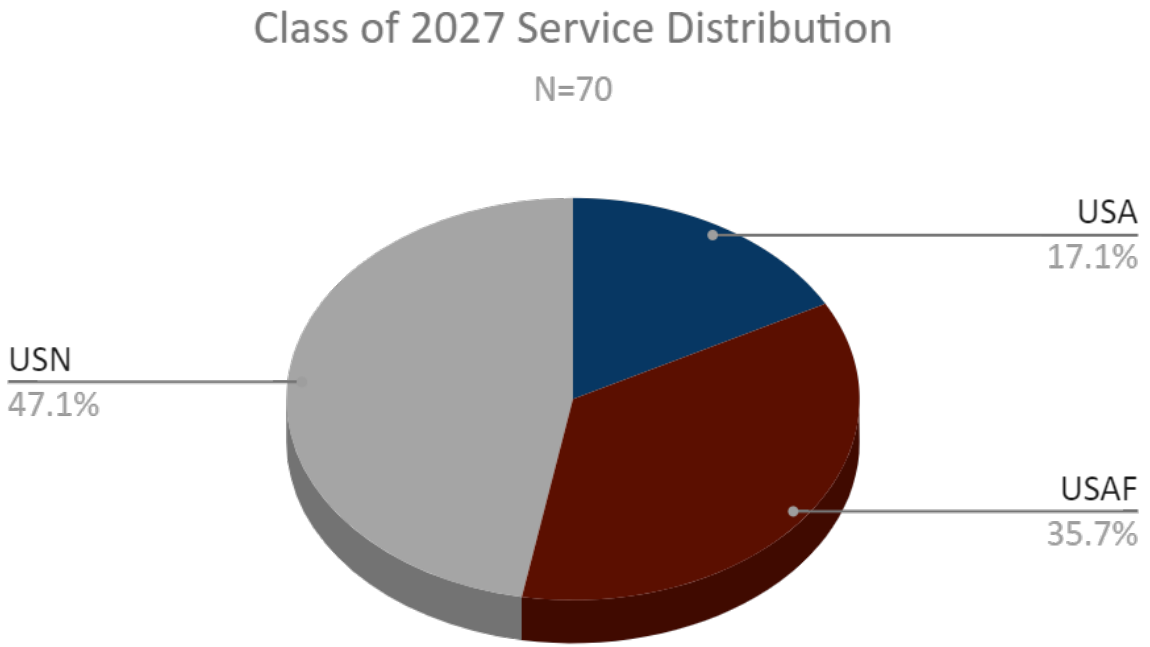
Graduating Students: Class of 2024

- 7 students qualify to be dual certified as both an FNP and WHNP.
- 100% board certification first time pass rates by our FNP and PMHNP students.
- WHNP, CRNA & AGCNS students cannot take certification exams until after graduation.

Matriculating Students: Class of 2027

(Matriculated 29 April, 2024)

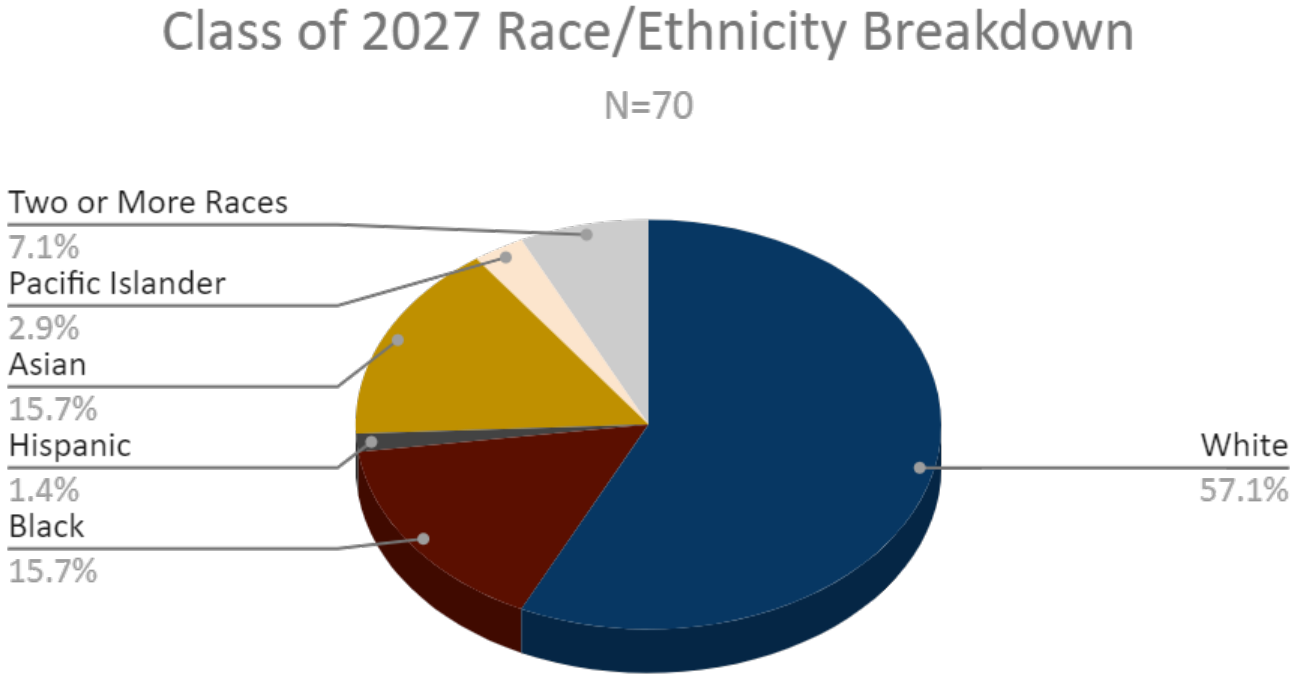




Graduate Nursing
Uniformed Services University

Matriculating Students: Class of 2027

- Class includes 3 Navy direct accessions and 2 Navy reservists (RNA & PMHNP)
- 11 students (16%) have prior service experience



Graduate Nursing
Uniformed Services University

New Initiatives:

- Nurse Anesthesia Accreditation Site Visit Review April 2024
  - results pending October Board Decision

- Interprofessional & Operational Education
  - Continue to expand- currently over 30 interactive course events
  - Operational medicine Bushmaster (mass casualty event)
  - Gunpowder (Prolonged field care) exercise expanded to all RNAs
  - Multiple operational electives in mountain & cold medicine.
    - Past year: 148 GSN students; 17 completed international diploma.
  - Trained Army 10th MTN and 11th Airborne Divisions, Navy Special Warfare, & Special Operations Command participants

New Initiatives:

- 2 faculty & 3 students joined the 86th Aeromedical Evacuation Squadron in Ramstein AB in a USEUCOM mission providing support to Critical Care Air Transport Team (CCAT) for over 30 injured patients from Germany to US Joint Base Andrews.

- Collaborations with
  - Val-de-Grace Military Academy, France;
  - Armed Forces Philippines Nursing Collaboration
  - Indian Health Service
  - America Samoa

Faculty

- Dr. Lynette Hamlin named as the Director of the USU Military Women's Health Research Program; expanded the MWHR database. DoD Delegate to the White House Women's Health Research initiative.
- Dr. Laura Taylor represented US at the United Nations' Commission on Status of Women, spoke on gender equality & equity in organ transplantation.
- Lt Col Regina Owen received APNA Award for Excellence in Leadership.
- MAJ Ken Romito inducted as Fellow in AORN
- LtCol David Bradley AMSUS Nurse of the Year

QUESTIONS?

TAB 5

End of Academic Year Summary

Postgraduate Dental College

USU Board of Regents
17 May 2024

End of Academic Year Report

Drew W. Fallis, DDS, MS, MHPE

Executive Dean, Postgraduate Dental College

USU
Uniformed Services University

Conflict of Interest / Disclosure

- I have no relevant financial or non-financial relationships to disclose relating to the content of this activity.

- The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Uniformed Services University, Department of Defense, nor the U.S. Government.

Outline

1. Outcome Metrics
2. Report of Students
3. Report of Faculty
4. Update on the PDC
5. Key Transformation Initiatives

Outcome Metrics

- Academic Outcomes – Strategic Measures of Performance
  - Accreditation (ADA CODA) of programs – **100%**
  - Graduation Rate (5 year avg) – **94.6%** *(Target; of 95%)*
  - On-time Graduation Rate – **99.3%** *(of 766 graduates, only 5 have required additional time)*
  - Written Board Certification Pass-rate (5 year avg) – **94%** *(Target; 90%)*
  - Graduates' Competency Satisfaction Rate – **92%** *(Target 90% completely or very effective)*
  - Supervisors' Satisfaction Rate – **93%** *(Target; 90% completely or very effective)*

Report of Students

- Academic Metrics for 2024
  - Number of MS in Oral Biology graduates (19 Programs) – **68** *(834 total with Class of 2024)*
  - Graduation Rate – **95.7%; 3 students withdrew from training** *(Target; of 95%)*
  - On-time Graduation Rate – **100%**

- 2024 Dr. Patrick B. Sculley Board of Regents Award Winner
  - CPT Aaron Colamarino (Periodontics, Fort Eisenhower)

"Influence of Lactobacillus reuteri, Bifidobacterium animalis subsp. lactis, and prebiotic inulin on dysbiotic dental biofilm composition ex vivo"

- Use of prebiotic Inulin *(plant fiber that improves gut health)* demonstrated statistically significant increases in good bacteria and decreases in pathogenic bacteria within periodontal biofilms

Report of Faculty

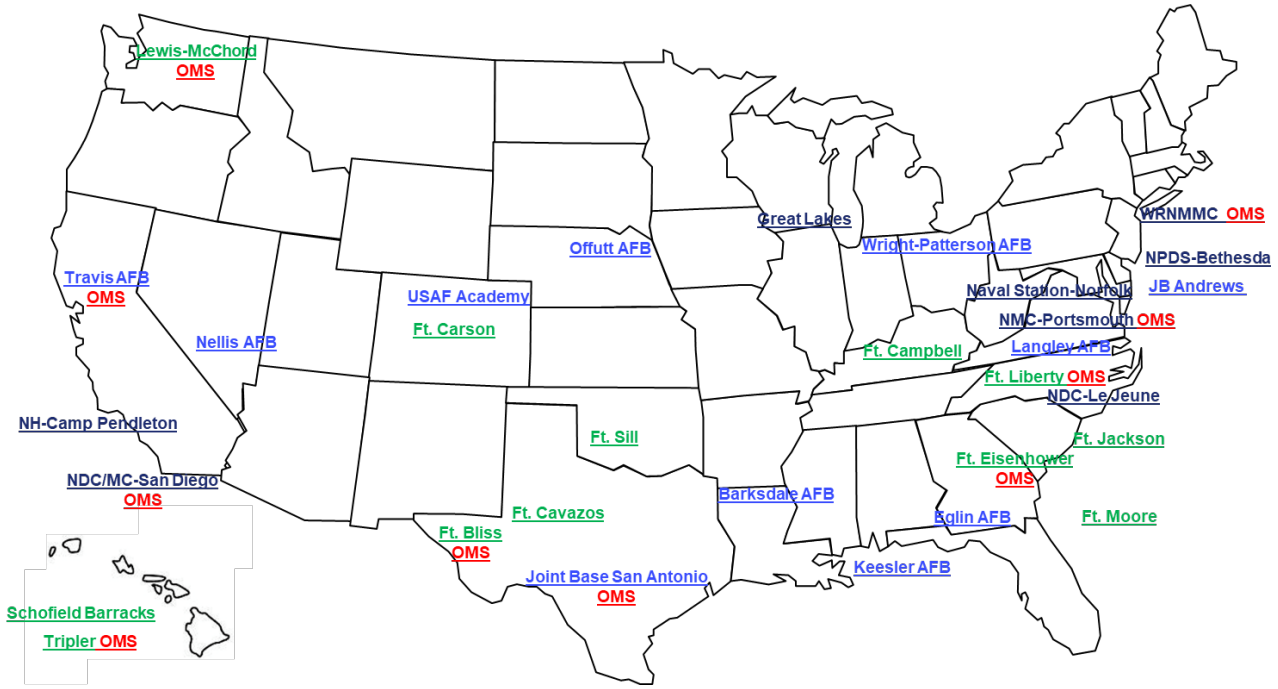
- Faculty Metrics
  - **Total** Faculty (non-billeted) – **501**
    - Junior Faculty (Assistant Prof) – **384** *(77%)*
    - Senior Faculty (Associate Prof and Prof) **– 117** *(23%)*
      - Professor – **49** *(42%)*
      - Associate Professor – **68** *(58%)*
  - **Completion** of Faculty Development Courses/Programs *(41: 8% of total faculty)*
    - American Dental Education Association (ADE) Academy of Academic Leadership – **6**
    - USU Faculty Development Certificate Programs – **20**
    - Stanford Clinical Instruction Certificate – **6**
    - USU Foundations in HPE Certificate – **5**
    - Degree completion: USU MHPE or MEd in HPE – **3** *(12 currently enrolled)*

Report of Faculty

- Federal Services Dental Educators Workshop (FSDEW)
  - 16-18 April, Bethesda (78 PDs/Dep PDs in attendance)

Update of the PDC

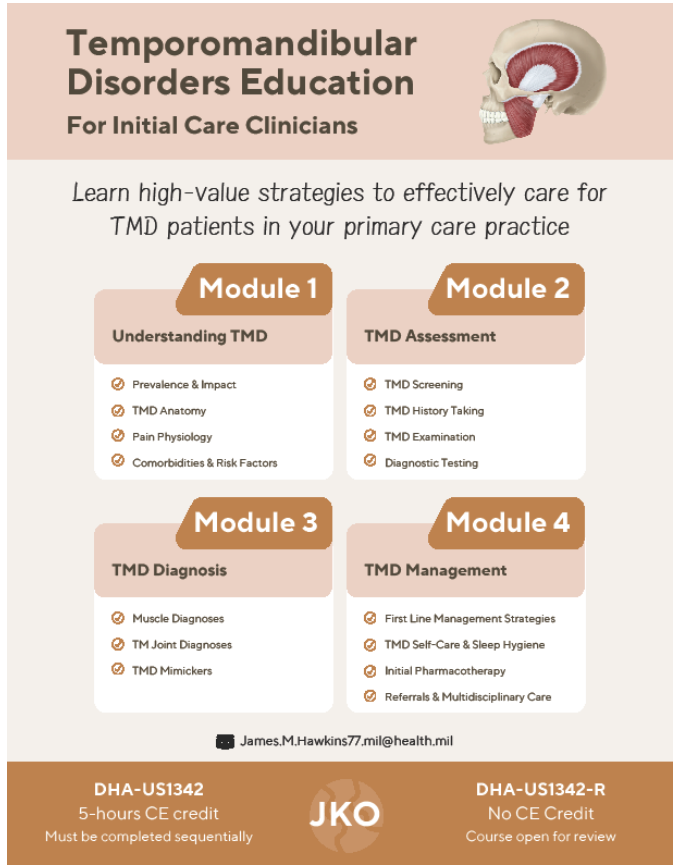
- Largest Portfolio of Graduate Dental Education (GDE) Programs in the Nation
  - 19 dental specialty programs (USU **MS degrees** in 7 mission-critical disciplines)
  - 26 PGY-1 certificate programs (USU affiliation for **curriculum and faculty development** support)
  - 10 OMS certificate programs (USU affiliation for **curriculum and faculty development** support)



USU
Uniformed Services University

Key Transformation Initiatives

- **Development of Standardized Digital Curriculum Support**
  - Research Methodology and Biostatistics curriculum to provide core subject content and multi-site access for all MS programs.
  - Standardized Oral Facial Pain Curriculum



Key Transformation Initiatives

- **Expansion of Tri-Service Center for Oral Health Studies (TSCOHS)**

  Leverage the unique PDC multi-site GDE structure to develop a Military Practice-Based Research Network (MPBRN).

  - Identify opportunities for multi-site Inter-Professional Research (IPR) projects integrating Medicine and Nursing.

https://www.facebook.com/photo/?fbid=2835978589835864&set=pcb.2835979686502421

Thank You….Questions?

TAB 6

End of Academic Year Summary

College of Allied Health Sciences

Uniformed Services University of the Health Sciences
Board of Regents

College of Allied Health Sciences Quarterly Board Report
17 May 2024

Submitted by: Andrew L. Reimund, Colonel (Ret.), USAF **Date: 18 April 2024**

Title & Department: Interim Dean, College of Allied Health Sciences **Phone: (210) 299-8527**

Purpose: Provide Quarterly Update **Information: Below** **Action: None**

Subject: College of Allied Health Sciences Quarterly Report

1. **Student Enrollment for Academic Year 2023-2024**

   The college continues to have great success with increased enrollments across its branch campus, the Medical Education and Training Campus, and other academic partners' locations (Naval Medical Forces Support Command, Medical Center of Excellence, Special Operations Center of Excellence, and the US Air Force School of Aerospace Medicine). New enrollments for the college's 27 programs reached 5919 students in the 2023-2024 Academic Year.

Service	Number of Students
Army, Army Reserve, Army National Guard	1534
Navy, Navy Reserve	3969
Air Force, Air Force Reserve, Air National Guard	398
Coast Guard	18
Total	**5919**

2. **Degree Conferrals Academic Year 2023-2024**

   College of Allied Health Sciences students earned 741 degrees prior to the May 2024 Commencement. The CAHS awarded the degrees in 21 different majors June 2023 to April 2024.

	June 2023 – April 2024 Graduations			
	Army	Navy	Air Force	Coast Guard
Associate of Science (644)	431	127	84	2
Bachelor of Science (97)	49	48	0	0

3. **Prospective Graduates for May 2024 Commencement**

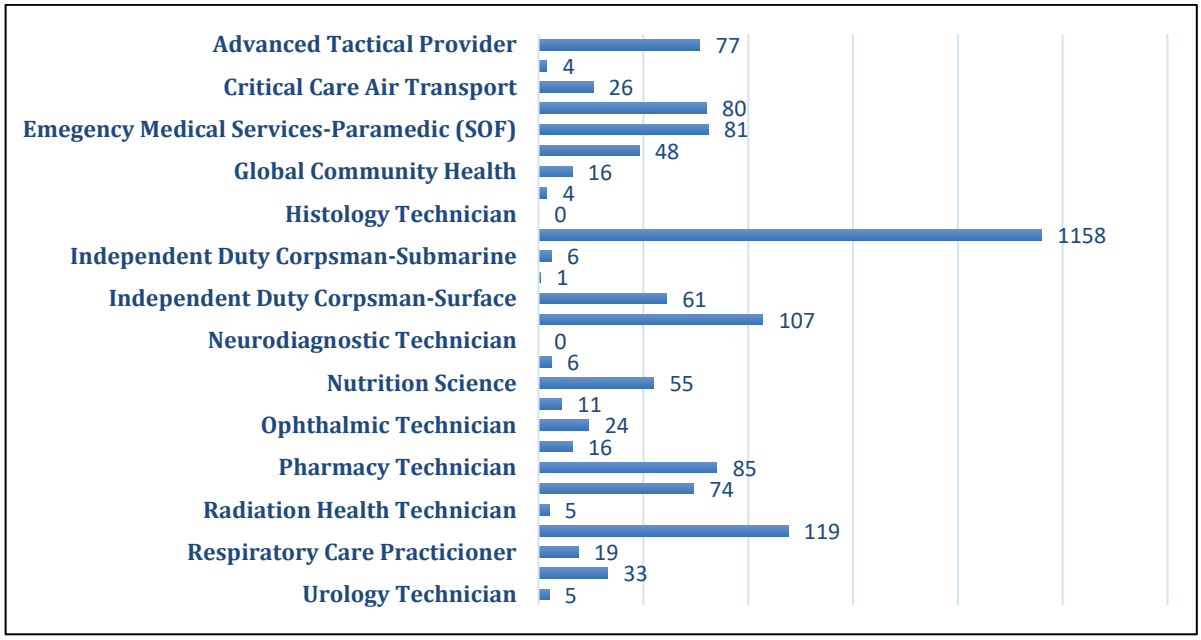
   As of 18 April, the CAHS is projecting a total of 310 graduates for the 18 May 2024 Commencement.

These students will be earning 73 Bachelor of Science and 249 Associate of Science degrees in 15 majors.

Degrees Projected for 2023				
	Army	Navy	Air Force	Coast Guard
Associate of Science (255)	164	52	37	2
Bachelor of Science (55)	25	30	0	0

4. **Training Program Completion for Fiscal Year 2024**

The CAHS faculty and staff have supported military department training requirements across its footprint. The first two quarters of Fiscal Year 2024 have seen 2121 students complete their service training programs, while earning college credit from the university. This number is a strong indicator that the CAHS will meet or exceed last fiscal year's number (5153) of student completions.



5. **Specialized Programmatic Accreditation**

The CAHS provides support for twelve programs holding specialized programmatic accreditation. Nine programs at the Medical Education and Training Campus (METC) branch campus are accredited. Other accredited programs within the CAHS network include: The Joint Special Operations Medical Training Center Paramedic Program and the Tri-Service Optician Course. Additionally, the Medical Center of Excellence Paramedic Program achieved full accreditation from the Committee on Accreditation of Educational Programs for the Emergency Medical Services Professions. The CAHS demonstrates commitment to maintaining high academic standards for all affiliated programs. This academic year, 100% of programs underwent successful annual programmatic reviews.

6. **Conclusion**

The College of Allied Health Sciences continues to demonstrate its value as a vital educational hub for military medical training. Strong enrollment numbers, a steady stream of graduates, and substantial training program completions underscore the college's success. Additionally, the college remains

committed to quality, reflected in ongoing accreditation efforts and successful programmatic reviews. While there will always be challenges to address, the college continues delivering its ongoing contributions to the professionalism and readiness of enlisted military medical personnel across all branches.

Uniformed Services University of the Health Sciences
Board of Regents Meeting
May 17, 2024

Andrew L. Reimund, Colonel (Ret.) USAF

Interim Dean, College of Allied Health Sciences

New Student Enrollment
CAHS Academic Year 2023-2024

Service	Students
Army, Army Reserve, Army National Guard	1534
Navy, Navy Reserve	3969
Air Force, Air Force Reserve, Air National Guard	398
Coast Guard	18
Total	**5919**

New enrollments for the college's 27 programs reached 5919 students in the Academic Year 2023-2024.

Degree Conferral
CAHS Academic Year 2023-2024

	Army	Navy	Air Force	Coast Guard
Associate of Science (644)	431	127	84	2
Bachelor of Science (97)	49	48	0	0

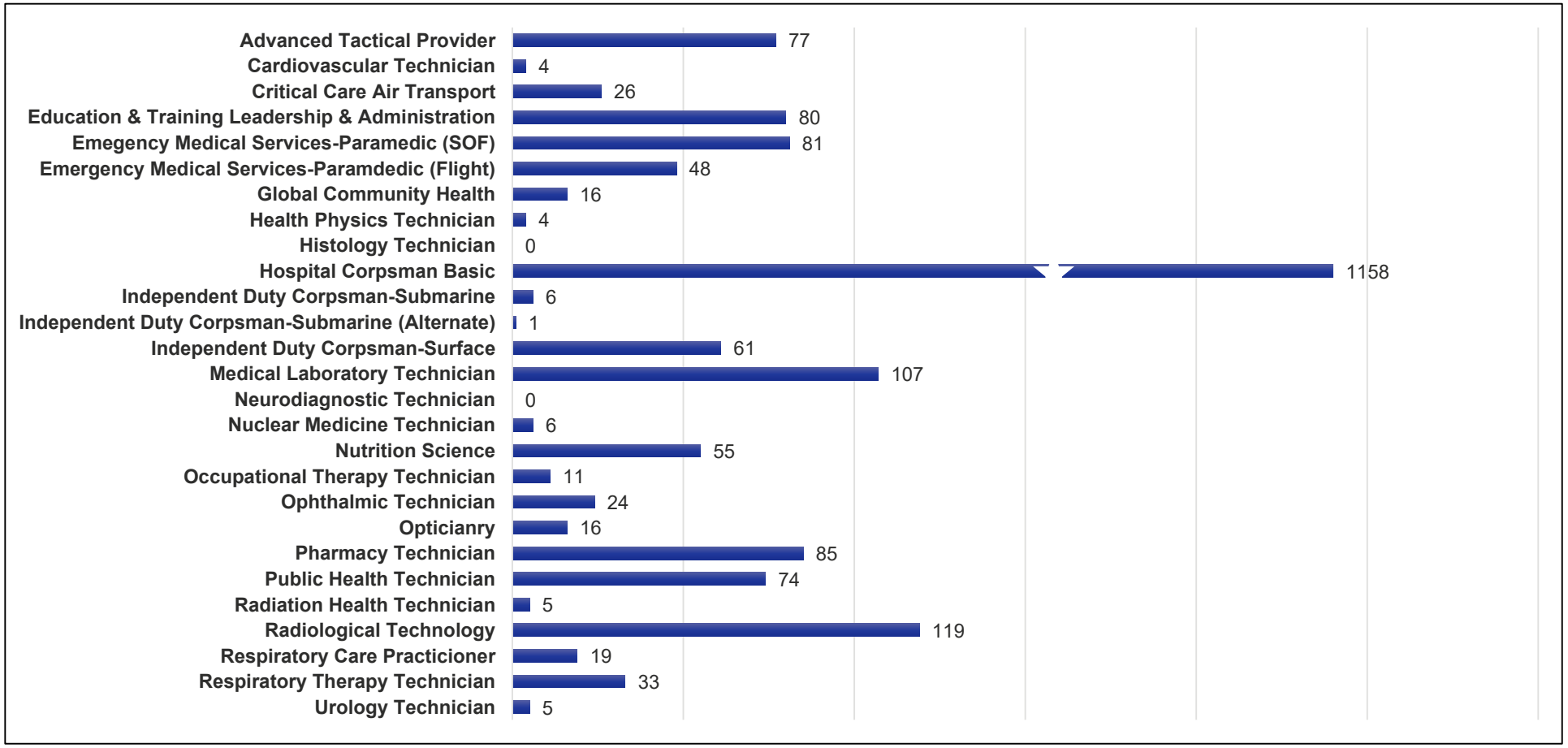
*Prior to the May commencement, the CAHS has awarded a total of 741 degrees. Our students have earned these degrees in 21 majors in the Academic Year 2023-2024.

Degree Conferral
CAHS Academic Year 2023-2024

Degrees Projected for May 2024				
	Army	Navy	Air Force	Coast Guard
Associate of Science (255)	164	52	37	2
Bachelor of Science (55)	25	30	0	0

*As of 18 April, the CAHS is projecting a total of 310 graduates for the May commencement. These students will be earning 55 Bachelor of Science and 255 Associate of Science degrees in 15 majors.

Training Program Completion
1st and 2nd Quarters Fiscal Year 2024



*The CAHS supported military training requirements seeing, in the first two quarters of the Fiscal Year, 2121 students completing their service training programs and earning college credit from the university.

Specialized Programmatic Accreditation

- The CAHS provided support for twelve programs with specialized programmatic accreditation.

  Medical Education and Training Campus – Nine Programs

  Joint Special Operations Medical Training Campus – One Program

  Tri-Service Opticians Course – One Program

- The Medical Center of Excellence's Paramedic Program achieved full accreditation from the Committee on Accreditation of Educational Programs for the Emergency Medical Services Professions.

- The CAHS monitored this status and conducts annual programmatic reviews for all affiliated programs; 100% have been reviewed this academic year.

Discussion

TAB 7

School of Medicine Admissions Process Update

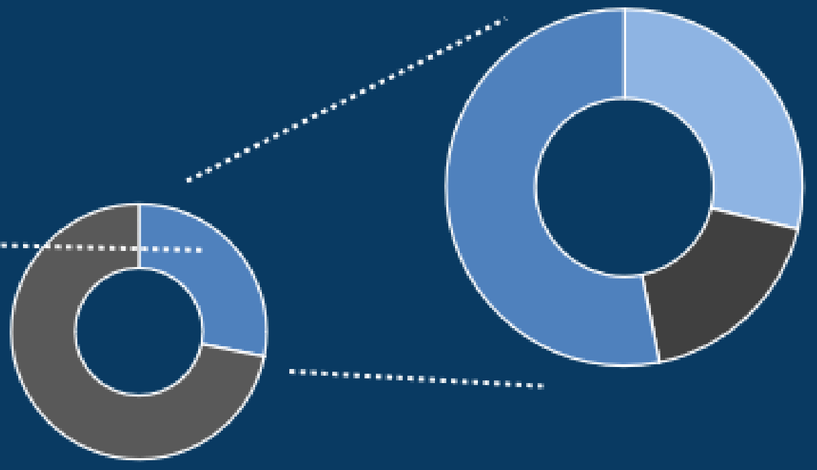
USU SOM ADMISSIONS

MAY 23-24

Danielle Holt, MD, MSS, FACS
Associate Dean for Admissions and Recruitment

Class of 2028*

- 2203 Applications
- 178 Positions
- 619 Interviewed
- 13% Acceptance Rate
- 290 Offers
- 61% Yield



Academics

- 3.7 GPA
- 3.7 Science GPA
- 510 MCAT
- 25 Graduate degrees

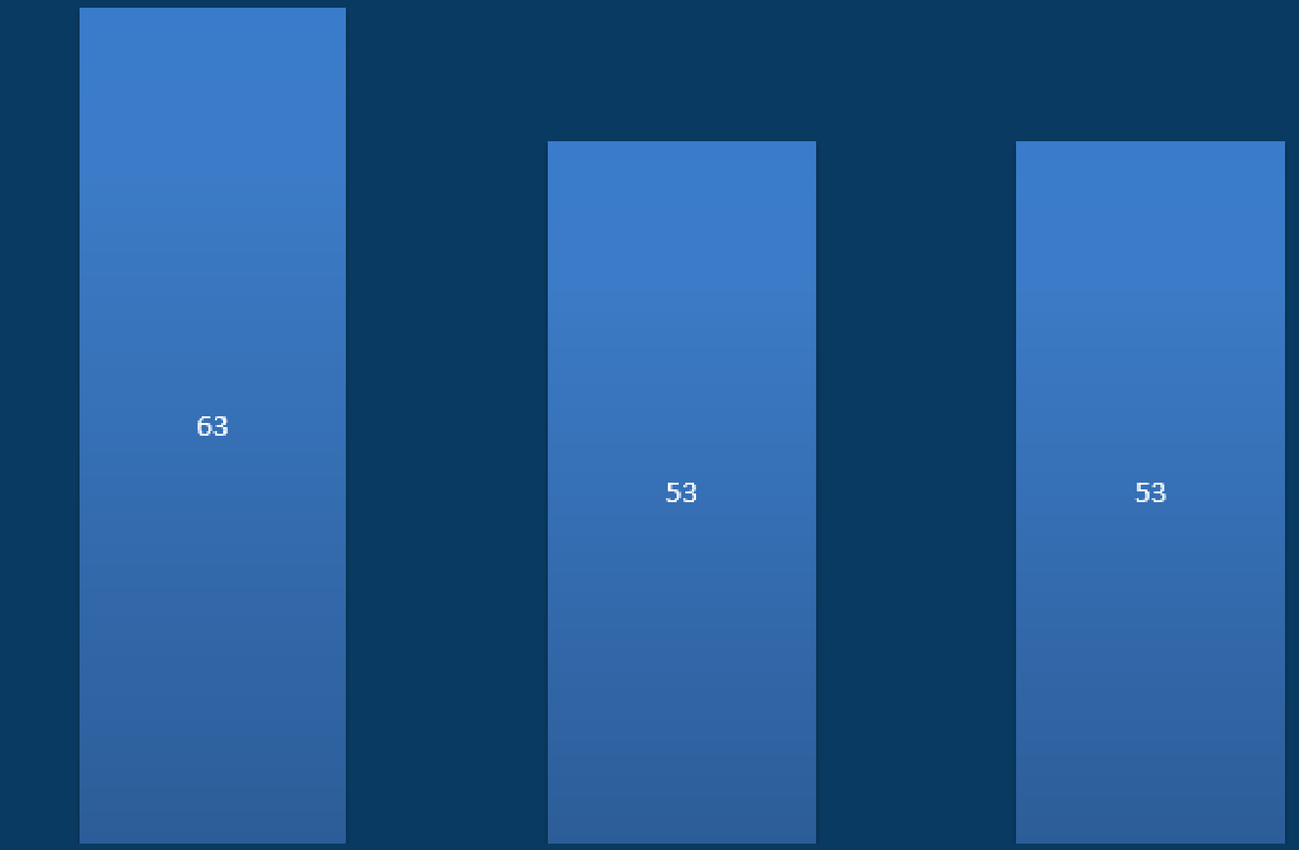
2 MD/PhD

17 EMDP2

as of 11 MAY

- 33% Nontraditional
- 22% SES disadvantaged
- 17% Reapplicants
- 10% First generation
- 25% College athletes
- 11 musicians
- 8 team captains

Class of 2028*



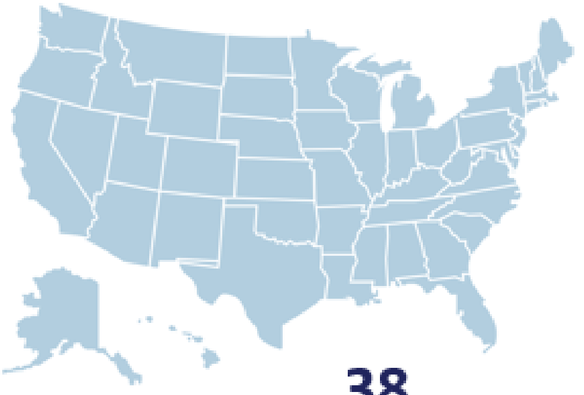
- 43% Women
- 17% URiM
- 19% Academy/ROTC
- 29% Veterans
  - 27 Enlisted
  - 24 Officers

Class of 2028*

- 29 - California
- 19 - Florida
- 19 - Maryland
- 18 - Texas
- 18 - Virginia
- 6 - New Jersey
- 5 - Pennsylvania
- 5 - Ohio
- 4 – New York
- 4 - Utah
- 4 - Colorado
- 3 - Massachusetts
- 3 – North Carolina
- 3 - Illinois
- 3 - Washington
- 3 - Michigan

- 61 - State Schools
- 12 - Ivy Plus
  - 5 - Johns Hopkins

- 7 - USMA
- 8 - USAFA
- 8 - USNA
- 12 - Military Colleges



38
states represented

**as of 11 May*

Admissions Process

Rolling

- First 120 files
- Accept by Committee
- Filled mid Nov

Selective

- 14/15 tertiary score
- URiM
- EMDP2

Waitlist

- Class full in January
- Conditional offers until March 15
- Prioritize by tertiary score, URiM

Commit to Enroll

- Medical and security clearance
- LOA for Active duty, Academy, ROTC
- April 30, no longer hold waitlist

Under-Represented in Medicine (URiM)

	All Hispanic	*Mexican*
Total URiM Applicants	484	406
URiM Applicants Interviewed	129	92
URiM Applicants Offers	70	54
URiM Applicants Declining	30	25
	23%	**16%**

Only 24 (20%) offers made during Rolling Admissions

Enlisted to Medical Degree Preparatory Program (EMDP2)

Cohort 5 (23 students)
USU Class of 2024

- 31 % women, 18% URiM
- Avg MCAT 504 (497-512)
- 75 % C5 Alumni completed in 4 years

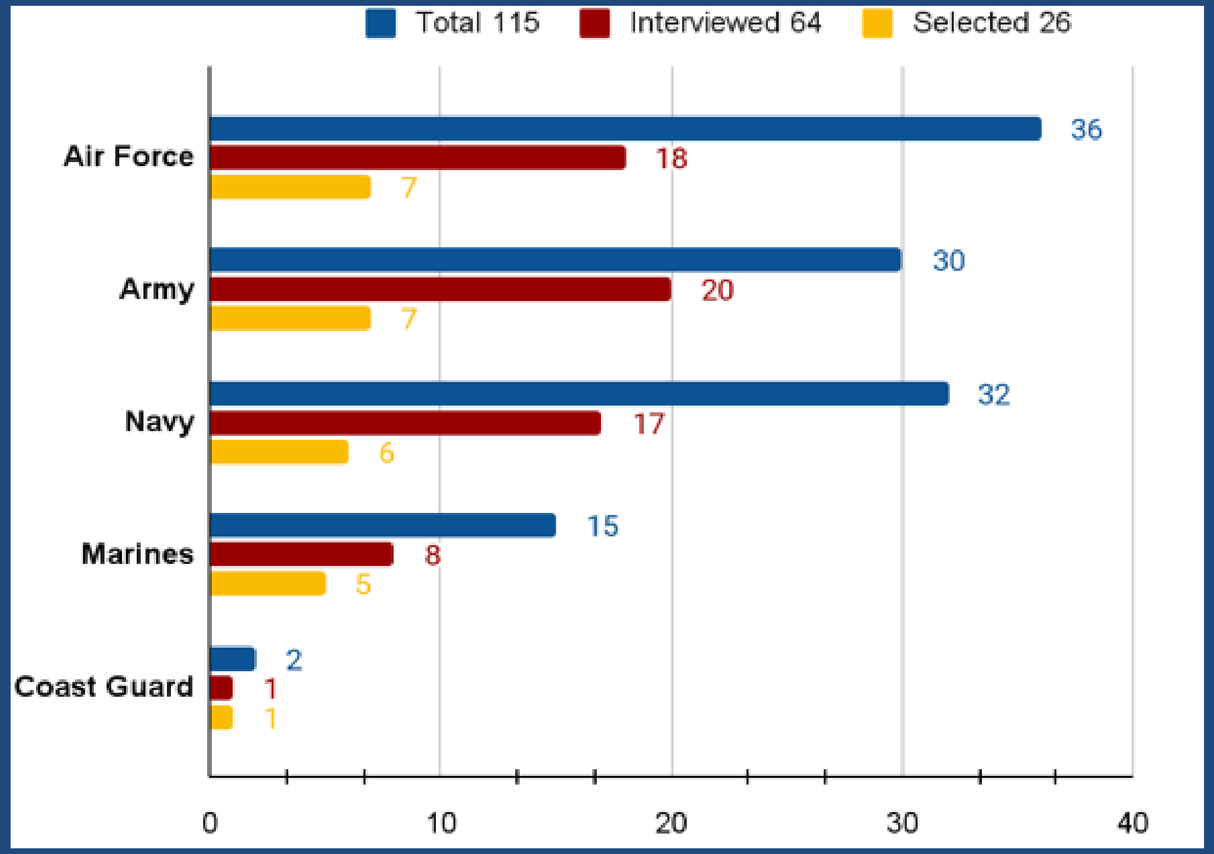
Cohort 9 (25 students)
Entering Medical School

- 32 % women, 36% URiM
- Avg MCAT 504 (486-512)
- 73% received acceptance (19)

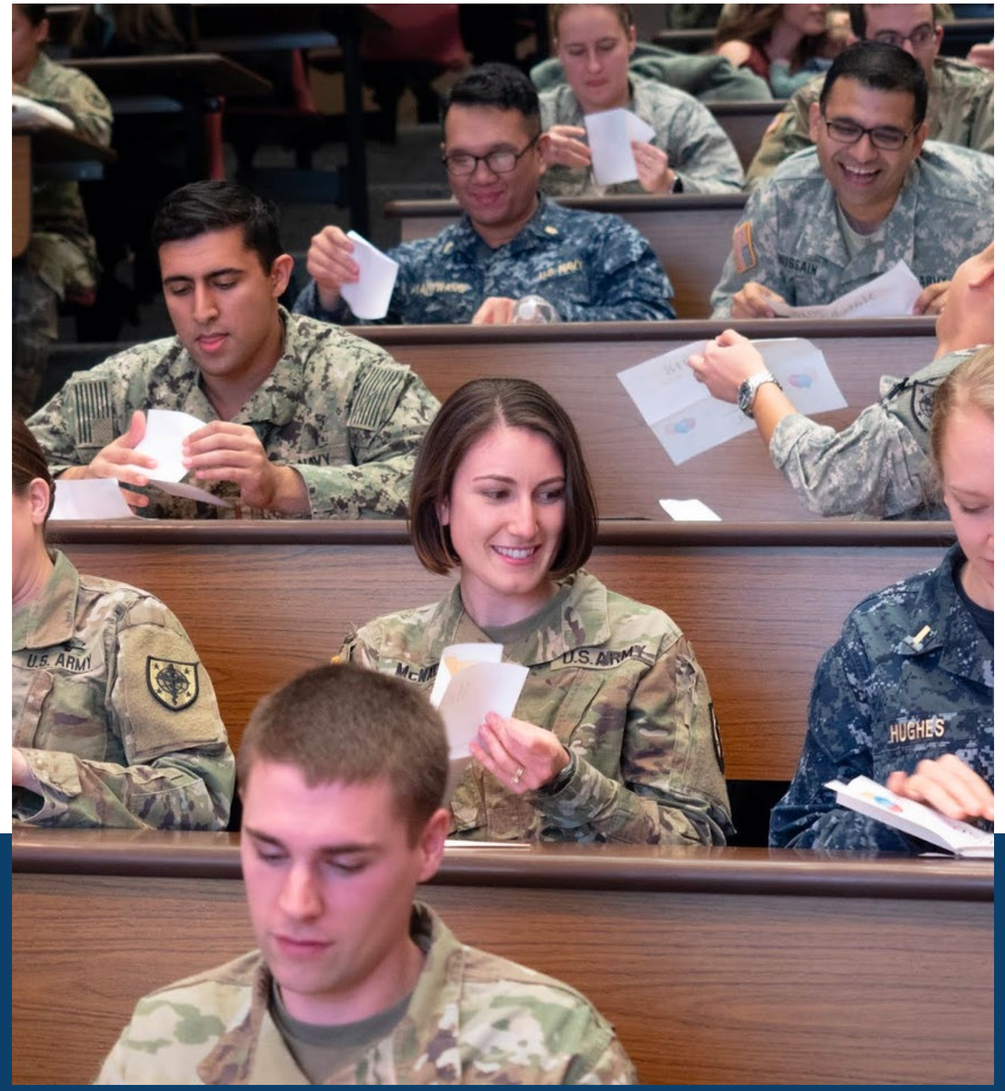
80 % EMDP2 Alumni matched in a Critical Wartime Specialty (13)

EMDP 2

Cohort 11 (26 students)
Entering EMDP2



- 30% women, 19% URiM
- Age 26-40 yrs
- Avg Undergraduate GPA 3.6 (2.7-4.0)
- Avg ACT 27.7 (20-32)
- Avg SAT 1335 (1110-1530)



Early Decision

- May 28: AMCAS application verification
- June 28: Application transmission to medical schools
- August 1: Early Decision Program application submission deadline
- October 1: Early Decision notification

NEW FOR AY 24-25

- Apply only to 1 school
- Released to regular applicant pool if not unconditional offer by 1 Oct

Admissions Process

Early Decision

- Notify by 1 Oct
- Release for Hold, Reject
- Continue rolling for first 100

Selective

- Starts Nov
- 14/15 tertiary score
- Prioritize URiM, EMDP2

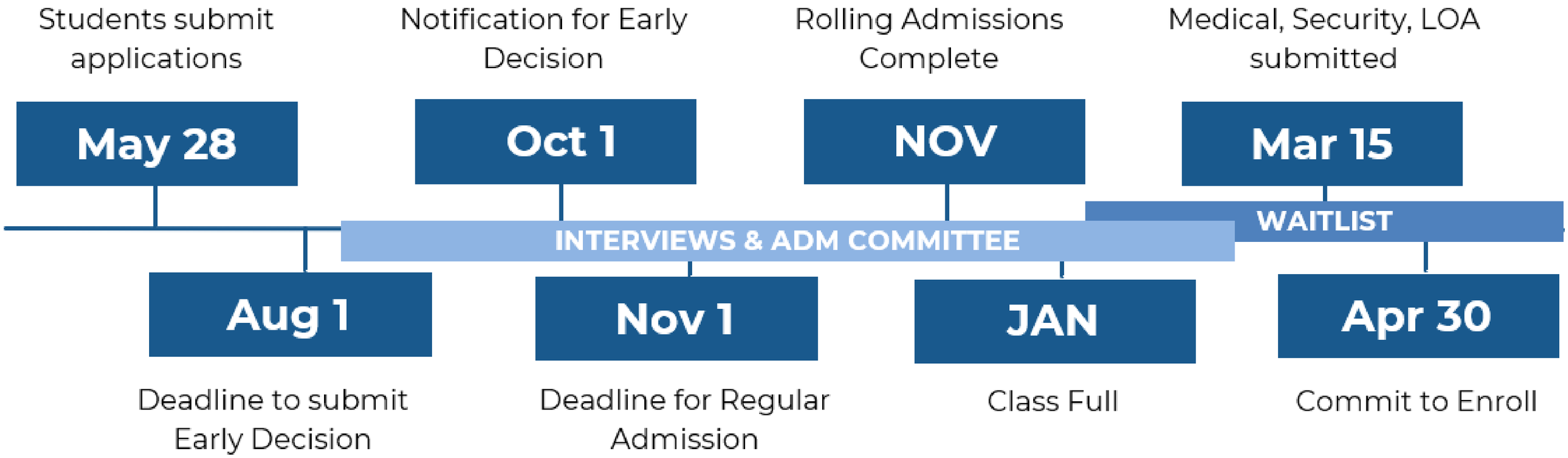
Waitlist

- Class full in Jan
- Conditional offers until March 15
- Prioritize by tertiary score, URiM

Commit to Enroll

- Medical and security clearance
- LOA for Active duty, Academy, ROTC
- April 30, no longer hold waitlist

Timeline


Students submit applications
May 28
Aug 1
Deadline to submit Early Decision
Notification for Early Decision
Oct 1
Nov 1
Deadline for Regular Admission
Rolling Admissions Complete
NOV
JAN
Class Full
Medical, Security, LOA submitted
Mar 15
Apr 30
Commit to Enroll
INTERVIEWS & ADM COMMITTEE
WAITLIST

Military Medical Ambassadors (MMA)

Program Goals

- Increase visibility of USU & extend geographic reach
- Represent USU as a modern, diverse medical school with superior education, research, and leadership development opportunities

Field representatives of military medicine

- 80% USU, 20% HPSP
- 70% Active duty, 20% Retired
- 34% Army, 33% Navy, 32% AF
- 70% Men, 28% Women, 2% Prefer not share
- 64% White, 11% Asian, 10% >1 selected, 4% Black, 1% Hispanic

https://medschool.usuhs.edu/resources

MMA

- 5% current students (24)
- Recently formed USU Student MMA Interest Group - SMMA
- Goal for students to remain as MMAs after graduation

National Capital Region (NCR), Mid-Atlantic, Texas & California make up ~70% of MMA

Region	n
Southeast	101 (22%)
Mid Atlantic	85 (18%)
Texas	71 (16%)
California	66 (14%)
Midwest	30 (7%)
South	25 (5%)
Southwest	23 (5%)
Pacific NW	20 (4%)
OCONUS	20 (4%)
Northeast	8 (2%)
Hawaii	3 (<1%)
Alaska	3 (<1%)
Northern Plains	3 (<1%)
Total	**458**

Matriculation Year

- 2027-2022 13%
- 2021-2016 18%
- 2015-2010 25%
- 2009-2004 14%
- 2003-1998 11%
- 1997-1992 9%
- 1985-1976 5%

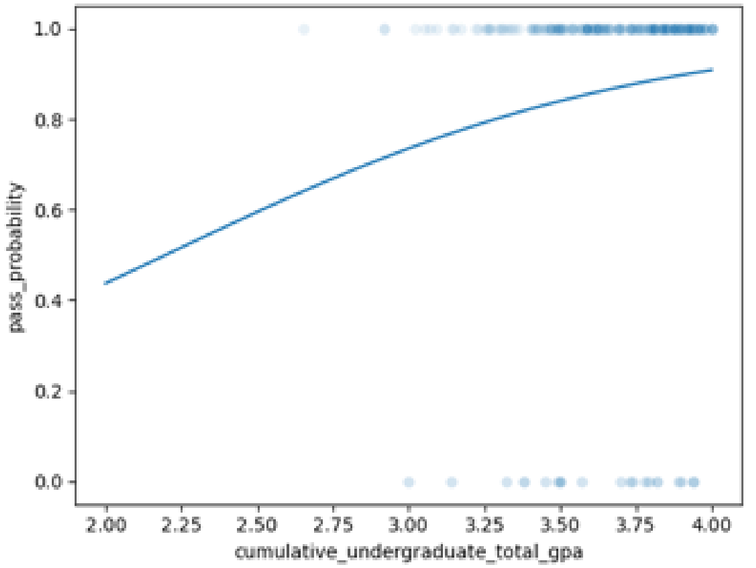
https://medschool.usuhs.edu/resources

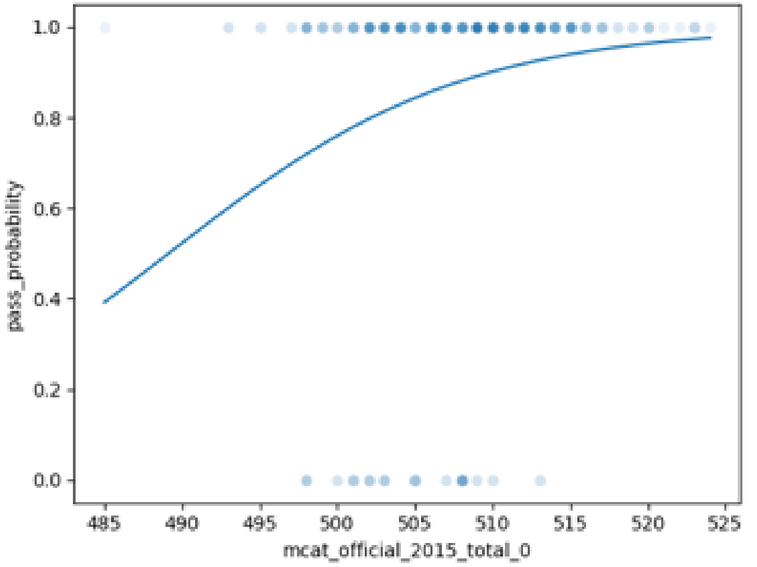
AI in Admissions

- Previously used regression model - NYU screening for interviews that closely match faculty recommendations
- How do undergrad GPA and MCAT scores predict passing both USMLE exams on first attempt
- Data from 2019-2022 matriculants

Artificial Intelligence Screening of Medical School Applications: Development and Validation of a Machine-Learning Algorithm

Marc M. Triola, MD, Ilan Reinstein, MS, Marina Marin, MSc, Colleen Gillespie, PhD, Steven Abramson, MD, Robert I. Grossman, MD, and Rafael Rivera Jr, MD, MBA





Preliminary results with ML model, requires further validation

Questions?

Danielle Holt, MD, MSS, FACS
Associate Dean for Admissions and Recruitment
danielle.holt@usuhs.edu

TAB 8

USU Accreditation Policy and Middle States Commission on Higher Education Update

USU Accreditation Update

Stephen Henske/Brian C. Rimm
Office of Accreditation

Uniformed Services University

17 May 2024

Recent Programmatic Accreditation Site visits

- School of Medicine – Liaison Committee on Medical Education
  - Site Visit - Jan 25-27, 2024
  - No finalized report yet- Draft Report noted no major deficiencies– see Dean Elster's Board Report
- School of Nursing – Commission on Collegiate Nursing/Council on Nurse Anesthesia Education
  - Site visit – April 16-18, 2024
  - No finalized report yet – Site Visit Team Out Brief noted no major deficiencies noted – See Dean Romano's Board Report

Status of MSCHE suggested improvements

- ***Standard VI - Planning, Resources, and Institutional Improvement,*** specifically focusing on:
  - 1. Adequate fiscal and human resources, including physical and technical infrastructure, to support operations.*
  - 2. Comprehensive planning for facilities, infrastructure, and technology that include consideration of sustainability and deferred maintenance. *
- Commission acknowledged receipt of the supplemental information report providing information on key data indicators (enrollment – FTE)

  * See details in Dr. Woodson's letter 01 March 2024 replying to the our MSCHE Vice President Liaison for corrective actions.

2024-25 Upcoming Reaccreditations

- The Accreditation Council for Graduate Medical Education (ACGME) - Spring 2024
- Commission on Dental Accreditation – CY 2025
  - Bethesda: Periodontics; Endodontics; Orofacial Pain; Prosthodontics; Advanced Education
  - Lackland AFB: Advanced Education in General Dentistry (24 months); Oral Maxillofacial Surgery (OMS); Periodontics
  - Ft. Gordon, GA: Periodontics; Oral Maxillofacial Surgery (OMS)
  - FT. Liberty, NC: Advanced Education in General Dentistry (24 months)

Recent MSCHE Accreditation Policy Changes

- ***April 5, 2024*** *:* The Middle States Commission on Higher Education (MSCHE) has developed the ***Information Security and Privacy Policy*** to formally establish an information security program with administrative, technical, and physical safeguards to protect information and prevent unauthorized access, use, modification, loss, destruction, dissemination, or disclosure of information.
- **New Accreditation Policy and Procedures:** *December 18, 2023* -The Commission has developed the Third-Party Providers Policy and Procedures to articulate the Commission's expectations for quality, integrity, transparency, and disclosure for institutions working with third-party providers. The policy and procedures also address written arrangements, which require approval prior to implementation through substantive…

Recent MSCHE Accreditation Policy Changes - Additions

- **The Commission will no longer pursue recognition with the Council for Higher Education Accreditation (CHEA),** which reflects a voluntary process that is not required for institutional accrediting agencies in the United States. The Middle States Commission on Higher Education continues to be recognized by the United States Secretary of Education, which is required.
- **Substantive Revision to Policy and Procedures Regarding MPPR and AIU**
- *June 30th, 2023*- The Commission made substantive revisions to the Accreditation Review Cycle and Monitoring Policy and Procedures, effective July 1, 2023. The purpose of this policy is to establish the timeline and components of the Commission's accreditation review cycle.

Questions

TAB 9

National Disaster Medical System
Pilot Program

National Disaster Medical System Pilot Program

Board of Regents

Jeffrey D. Freeman, PhD, MPH
Director | Special Assistant to the President
National Center for Disaster Medicine and Public Health
Uniformed Services University of the Health Sciences

NCDMPH

Uniformed Services University

Est 2008

The National Center for Disaster Medicine and Public Health (NCDMPH) was established under Homeland Security Presidential Directive-21 (HSPD-21)

- Both a federal organization and academic center
- Based at the Uniformed Services University
- Supporting role to the federal interagency
- Partnership between DoD, HHS, DHS, DoT, VA, and DoS

Image Credit: Smiley N. Pool/The Dallas Morning News

NCDMPH
Uniformed Services University

Board of Advisors

Dr. David J. Smith
Deputy Assistant Secretary of Defense, Health Readiness Policy and Oversight, DoD

Stephanie Koeshall
Principal Director, Homeland Defense Integration and Defense Support of Civil Authorities, DoD

Derrick K.S. Jaastad
Executive Director, Office of Emergency Management, VHA

Jonathan N. Greene
Deputy Assistant Secretary, Office of Response, Administration for Strategic Preparedness and Response, HHS

Dr. Henry Walke
Director, Office of Readiness and Response, Centers for Disease Control and Prevention, HHS

Dr. Hillary Carter
Principal Deputy Coordinator, Bureau of Global Health Security and Diplomacy, DoS

Dr. Harveen Bergquist
Director, Operational and Protective Medicine, Bureau of Medical Services, DoS

Donna O'Berry
Deputy Director, Office of Intelligence, Security and Emergency Response, DoT

Dr. Herbert Wolfe
Acting Chief Medical Officer, Acting Director, Office of Health Security, DHS

Matthew Payne
Deputy Assistant Administrator, Office of Response and Recovery, Federal Emergency Management Agency, DHS

Mission

To advance the Nation’s medical and public health readiness for disasters

National Program

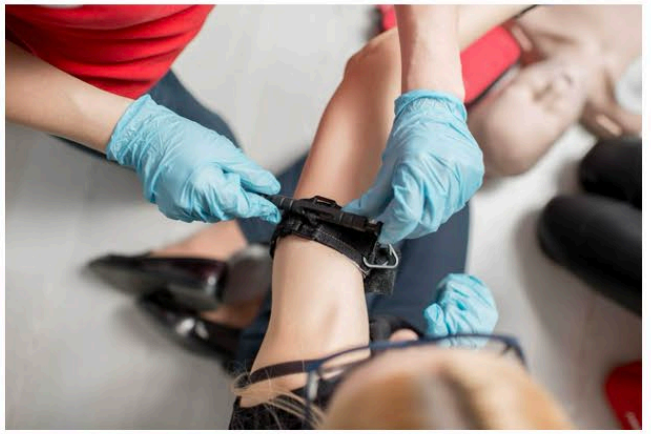
Disaster Medicine and Public Health

Science

DATA TO DECISIONS

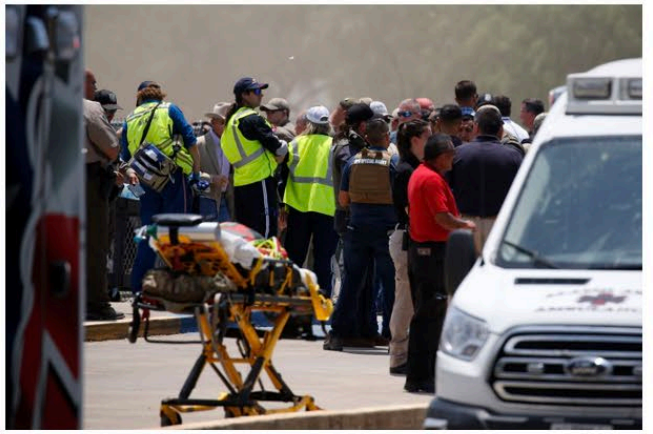
Operations

DECISIONS TO IMPACT



Education

SUSTAINED EXCELLENCE



Strategic Emphasis

NCDMPH
Uniformed Services University

The National Center's

Joint Disaster Medicine and Public Health Ecosystem

has been established to serve as a national resource for advancing the Nation's readiness for disasters and other health emergencies. The ecosystem is comprised of leading organizations across government, academia, and industry that have demonstrated excellence in disaster medicine and public health.

Ecosystem in Practice

NDMS Origin

- Created by Congress in 1984 for Cold War repatriation mission
- Partnership between DoD, VA, DHS, and HHS
- Three primary missions
  1. Medical response
  2. Patient movement
  3. Definitive care
- 3,800 federal intermittent employees
- 40 DMAT (10 on call per month)
- Never been used for large-scale combat operations

NCDMPH
Uniformed Services University

NDMS Pilot Program

Congressionally directed program to enhance interoperability and expand capabilities of the NDMS (DoDI 6010.22)

THE PILOT IS REQUIRED TO:

- Address the requirements of a LSCO or catastrophic event in the homeland
- Establish partnerships with public and private healthcare organizations
- Ensure coordination with the Federal Interagency
- Be conducted over five years at no less than five sites

The National Center for Disaster Medicine and Public Health was chosen as the Office of Primary Responsibility

[1]Kirsch, Thomas D., et al. "Validation of Opportunities to Strengthen the National Disaster Medical System: The Military–Civilian NDMS Interoperability Study Quantitative Step." *Health security* (2023).

Image Credit: Health.mil

NCDMPH
Uniformed Services University

NDMS Pilot Execution

Pilot site projects are directed by NCDMPH and executed by

- Pilot site-based field implementation teams (FIT)
- Regional academic partners
- Health care industry partners

Pilot site stakeholders include

- Federal ESF-8 partners
- State ESF-8 partners
- Local ESF-8 partners
- DoD and VA Federal Coordinating Center leadership
- Civilian hospitals, post-acute care facilities, etc.

Sacramento, CA	Denver, CO	Omaha, NE	San Antonio, TX	National Capital Region

NCDMPH
Uniformed Services University

NDMS Pilot Activities

SITE PROJECTS

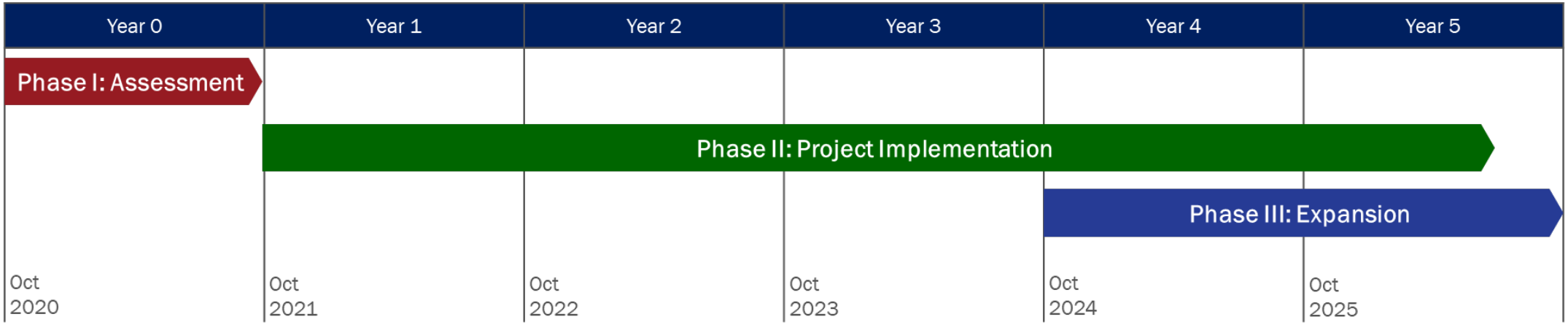
Site projects are designed to develop, test, validate, and scale potential solutions aimed at improving the capacity and interoperability of the NDMS.

NATIONAL STUDIES

National studies are designed to investigate key constraints and identify areas of opportunity for meeting the medical requirements of a LSCO.

EXERCISES

Pilot exercises, which include tabletop, functional, and full-scale exercises, are designed to identify needs and assess the effectiveness of adopted solutions.



NDMS Pilot Support to ICMOP

NCDMPH Support to USNORTHCOM in FY2023

- ICMOP Base Level II Plan support including mission analysis development, commander's estimate development and exercise planning
- Action Officer support for ICMOP stakeholders
- USNORTHCOM participation in Pilot Year 2 stakeholder meeting and Denver site tabletop exercise
- ICMOP process flow development and comment resolution matrix analysis

Support to USNORTHCOM in FY2024

- Continued staffing support to USNORTHCOM J5
- Level III concept plan development
- Force Flow conference with USTRANSCOM and key ICMOP stakeholders
- Tabletop exercise with the Defense Health Agency
- Reserve medical staffing and case management research projects to evaluate mission analysis gaps and inform Level III planning

NDMS Pilot Impact Summary

- Five sites have been fully staffed and coordinated with federal, state, local, academic, and industry partners (ability to flex)
- Pilot continues to provide full time staff to USNORTHCOM to support ICMOP development
- Site implementation teams are providing direct support to FCCs, including alignment to ICMOP, updating FCC patient reception plans, and expanding MIL-CIV partnerships
- 10 exercises have been completed across the five Pilot sites
- Other highlights
  - To ensure unity of effort, NDMS Pilot team briefs with USNORTHCOM during monthly in-progress reviews to the JSS
  - Reserve manpower study being conducted in coordination with DoD Homeland Defense Integration and DoD P&R
  - EMS capacity study being conducted in direct coordination with FEMA and ASPR
  - Full review of all current NDMS Pilot activities is underway and being coordinated with the interagency
  - Summary report and deliverables on all initial NDMS Pilot projects currently in development (available NLT Q1 FY25)

A Fundamental Challenge

Large-scale combat operations will require medical resources well above what can be sustained under steady state.

NDMS Pilot Improvements

Our objective is to achieve a sustainable model for military and civilian medical readiness by strengthening interoperable partnerships and enhancing the capacity and agility of the National Disaster Medical System.

Goal 1

ASSESS AND STRENGTHEN THE NDMS OF TODAY

Goal 2

DEFINE POLICY RECOMMENDATIONS FOR IMPROVING THE NDMS OF TOMORROW

Goal 3

DEVELOP PLANS FOR RAPIDLY GROWING THE NDMS UNDER FUTURE SCENARIOS

The NDMS Pilot is designed to address the limitations our military and civilian health systems must overcome in preparing for large-scale events. We aim to address these constraints by: (1) assessing and strengthening our current health systems, (2) defining policy recommendations for improving future health systems, and (3) developing operational plans to facilitate rapid capacity building during large scale events requiring resources above what can be sustained under routine operations.

FY24-25 Pilot Priorities

Considerations and Path Forward

- Pilot has been very active, but must focus to enable scale
  - Comprehensive NDMS Pilot Program Review with the Interagency
- Initial assessment was qualitative only
  - System modeling for a LSCO mission with MIT Lincoln Lab
- Policy review and recommendations will have broad implications
  - Policy Review with Georgetown University and the Library of Congress
- Pilot program should be representative, operational, and sustainable
  - Expansion to potential MIL-CIV innovation hubs in alignment with ICMOP
- Current efforts alone will not overcome the principal challenge in disasters
  - Building on the Fly by Design

NCDMPH
Uniformed Services University

Thank you

NCDMPH
Uniformed Services University

Supplement

TAB 10

Postgraduate Dental College

Uniformed Services University of the Health Sciences
Board of Regents

Board Brief

Submitted by: **Drew W. Fallis, DDS, MS, MHPE** **Date:** **17 May 2024**

Title/Department: **Executive Dean, Postgraduate Dental College (PDC)** **Phone:** **210-260-5094**

Purpose: **Information** **X** **Action** _____

Subject: **PDC Dean's Report**

Report Areas:

1. Program Metrics:
   - 19 MS-level dental specialty residencies
     -- Accreditation (ADA CODA) of programs: 100% *(target of 100%)*
     -- Graduation Rate (5 year avg): 95% *(target of 95%)*
     -- On-time Graduation Rate: 99.3% *(target of 95%; only 5 of 766 graduates extended)*
     -- Written Board Certification Rate: 94% *(target of 90%)*
     -- Graduates' Competency Satisfaction Rate: 92% *(target 90%)*
     -- Supervisors' Satisfaction Rate: 93% *(target 90%)*
   - 26 PGY-1 program affiliations
   - 10 Oral and Maxillofacial Surgery (OMS) program affiliations

2. PDC Students:

   - Sixty-eight Army (32), Navy (17), and Air Force (19) students at the six PDC-affiliated training locations are projected to earn Master of Science in Oral Biology degrees in 2024. Graduates will receive diplomas, pending completion of all degree requirements and approval by the President, USU. At the completion of this academic year, USU will have awarded a total of 833 Masters of Science degrees to program graduates.

   - Seventy-three students have been matriculated into the MS in Oral Biology Program and will start their specialty residency programs on 1 July 2024. These students include 38 Army (4 in AFPDS residencies), 21 Navy (2 in AFPDS residencies), 13 AF, and 1 Canadian (AFPDS Periodontics residency).

   Student Research Activities: Dr. Rodney Phoenix, Associate Dean for Dental Research (ADDR)

- 71 project entries from 19 master's degree postgraduate dental residency programs were submitted to the annual Tri-Service Dental Research Competition. The Army, Navy and Air Force Postgraduate Dental Schools then identified one research project to compete for the Dental Research Award. A panel of USU senior researchers representing the Postgraduate Dental College, School of Medicine, and Graduate School of Nursing selected the top project and oral presentations were conducted on 17 April 2024 during the Federal Services Dental Educators Workshop (FSDEW) on the main USU campus, Bethesda.

CPT Aaron Colamarino (2023 graduate of the US Army Periodontics residency at Fort Eisenhower, Georgia) was selected as the 2024 winner for his research project entitled *"Influence of Lactobacillus reuteri, Bifidobacterium animalis subsp. lactis, and prebiotic inulin on dysbiotic dental biofilm composition ex vivo"*. (attached thesis)

3. Faculty activities: Dr. Jay Graver, Associate Dean for Faculty Affairs (ADFA)

   - The ADFA organized and conducted the 2024 Federal Services Dental Educators Workshop on the main USU campus, Bethesda, 16-18 April 2024. 78 military dental educators, representing 48 graduate dental education programs across the US were in attendance to share best practices and develop collaborative initiatives.

4. Tri-Service Center for Oral Health Studies (TSCOHS) activities/initiative:

   - A current initiative is the development of a military practice-based research network (MPBRN) to optimize multi-site dental public health research across PDC residency program locations utilizing USU faculty.

Current & Future Concerns: None, at this time.

Funding/Budget Estimate/Fiscal Impact: None

Staffing Impact: None

Board Action Requested: None

Influence of *Lactobacillus reuteri*, *Bifidobacterium animalis* subsp. *lactis*, and prebiotic inulin on dysbiotic dental biofilm composition ex vivo

by

Aaron N. Colamarino, DDS

CPT, DC, USA

Thesis directed by:

Thomas M. Johnson, DMD, MS; COL, DC, USA
Professor, Department of Periodontics, Army Postgraduate Dental School

Thesis committee members:

Daniel M. Boudreaux, PhD; MAJ, MS, USA
Department of Clinical Investigation, Dwight David Eisenhower Army Medical Center

Joseph M. Dutner, DMD, MS; LTC, DC, USA
Associate Professor, Department of Endodontics, Army Postgraduate Dental School

Brian W. Stancoven, DMD, MS; LTC(P), DC, USA
Associate Professor, Department of Periodontics, Army Postgraduate Dental School

Adam R. Lincicum, DMD, MS; LTC(P), DC, USA
Assistant Professor, Department of Periodontics, Army Postgraduate Dental School

Thesis submitted to the Faculty of the
Army Postgraduate Dental School
Postgraduate Dental College
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Master of Science 2023

Army Nominee
CPT Colamarino

ABSTRACT

Background: Probiotic bacterial supplementation has shown promising results in the treatment of periodontitis and the maintenance of periodontal health. The purpose of this investigation was to evaluate the influence of *Lactobacillus reuteri* or *Bifidobacterium animalis* subsp. *lactis* supplementation with and without prebiotic inulin on biofilm composition using an ex vivo biofilm model.

Methods: Subgingival plaque specimens from three periodontitis-affected human donors were used to grow biofilms on hydroxyapatite disks in media supplemented with varying combinations of prebiotic inulin, *Lactobacillus reuteri,* and *Bifidobacterium animalis* subsp. *lactis*. Relative abundances of bacterial genera present in mature biofilms were evaluated using 16S rRNA next generation sequencing. Diversity metrics of microbial communities were evaluated using a next-generation microbiome bioinformatics platform.

Results: Inulin supplementation produced statistically significant dose-dependent increases in relative abundances of *Lactobacillus* and *Bifidobacterium* species ($p<0.001$) with concomitant decreases in relative abundances of *Streptococcus, Veillonella, Fusobacterium, Parvimonas,* and *Prevotella* species ($p<0.001$). Inoculation with *L. reuteri* or *B. animalis* subsp. *lactis* increased the relative abundance of only the supplemented probiotic genera ($p<0.05$). Supplemental inulin led to a statistically significant decrease in biofilm alpha diversity ($p<0.001$).

Conclusions: The described ex vivo model appears suitable for investigating effects of probiotic bacteria, prebiotic oligosaccharides, and combinations thereof on biofilm composition and complexity. Within the limitations imposed by this model, results from the present study

underscore the potential for prebiotic inulin to modify biofilm composition favorably. Additional research further elucidating biologic rationale and controlled clinical research defining therapeutic benefits is warranted.

KEY WORDS: Periodontitis, biofilms, dental plaque, probiotics, prebiotics, inulin

INTRODUCTION

For almost a half century, researchers have understood that the microbial cells colonizing the human body typically equal, or possibly far exceed, the somatic cell count.[1-3] Indeed, our microbial cohabitants are abundant and diverse. A healthy human may accommodate between 500 and 1000 bacterial species at any given time.[4] However, the mixture and relative abundance of bacterial species inhabiting various dermal and mucosal sites exhibit temporal variations, and individual patients may harbor profoundly different microbial collections.[1,3] For example, only about one third of the gut microbiota appears common to most humans, whereas the remaining two thirds comprises species that are specific to the individual.[3] Although some determinants of temporal and inter-individual microbiome variability are known, investigators do not fully understand the influence of these variations on health, wellness, and the onset/progression of disease.[1] Nevertheless, unfavorable changes in the microbiome—with associated immune, endocrine, and nervous system interactions—correlate with an array of human afflictions including inflammatory bowel disease, cancer, sinusitis, and periodontitis.[5-9]

Given the abundance and biodiversity of the human microbiome, it is unsurprising that manipulation of its composition—physically or pharmacologically—is an important strategy in the prevention and treatment of many diseases. In 1954, Kragen became the first author to report inoculation of the oral cavity with a beneficial bacterial species.[10] Lilly and Stillwell introduced the term "probiotics" in 1965,[11] and the World Health Organization subsequently established the widely accepted definition "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host."[12] In recent years, investigators have

utilized oral probiotics to treat or prevent dental caries, *Candida* infections, halitosis, and periodontal disease.[13,14] Dental practitioners have delivered these supplements as powders, suspensions, capsules, lozenges, and foods fortified with specific probiotic strains.[14]

New concepts in periodontitis etiopathogenesis may bolster interest in the therapeutic potential of oral probiotics. Periodontitis is an archetypical multifactorial disease process, whereby periodontal tissue destruction manifests through complex interactions between environmental and genetic factors.[8,9] Although genetic influences account for half of the variability associated with periodontitis,[15] behavioral and environmental factors emerging over the last two centuries appear responsible for a sudden surge in the prevalence of the disease.[9] For decades, investigators have associated the presence of *Porphyromonas gingivalis* and *Tannerella forsythia* in subgingival biofilms with increased risk of developing periodontitis, increased risk of progression to advanced disease, and decreased likelihood of successful treatment.[16] However, ample evidence now suggests that periodontitis results not from one or a few bacterial species but from true polymicrobial activity.[8] Accordingly, probiotics may benefit the host through a variety of mechanisms including competitive inhibition of pathogens, suppression of virulence factors, augmentation of the mucosal barrier function, development of the immune system, host immunomodulation, and synthesis of antimicrobial peptides.[17,18]

Researchers have characterized microbiological and clinical effects of numerous probiotic strains. Of these, *Lactobacillus reuteri* and *Bifidobacterium animalis* subsp*. lactis* have shown promising results in the treatment and prevention of periodontal disease with high safety margins.[18-30] *L. reuteri* is an indigenous microorganism of the human gastrointestinal

tract known to modulate cytokine levels, suppress inflammation, and produce reuterin, an antimicrobial protein.[30, 31] In randomized controlled trials, *L. reuteri* supplementation has reduced the presence of specific periodontal pathogens, decreased levels of cytokines and other inflammatory markers, and improved periodontitis treatment outcome measures such as probing depth, clinical attachment level, plaque index, gingival index, and bleeding on probing.[18, 19-22] *B. animalis* subsp. *lactis* is also considered a normal resident of the human microbiome, exhibiting a symbiotic relationship with the host through antimicrobial and immunomodulatory properties.[23] In an in vitro study, probiotics of the *Bifidobacterium* genus increased IL-10 levels and inhibited IL-1b and TNF-α effects.[24] In randomized controlled trials and rodent models, *B. animalis* subsp. *lactis* supplementation has decreased pro-inflammatory and increased anti-inflammatory cytokine levels, reduced the relative abundances of orange- and red-complex bacteria, and produced clinical benefits comparable to those described for *L. reuteri*.[13, 23-27]

A technical challenge limiting the clinical application of oral probiotics for therapeutic and preventative purposes is the inability to establish beneficial species as prominent members of the host microbiota without consistent inoculation. Although *L. reuteri* and *B. animals* subsp. *lactis* are capable of surviving in oral biofilms,[25] most researchers agree that colonization of these species is transient without sustained/repeated intake.[21, 28, 29] Efforts to overcome this obstacle have led to studies involving prebiotics—non-digestible oligosaccharides that promote proliferation of beneficial commensal species.[32] Three criteria have been proposed for classifying a carbohydrate as a prebiotic: 1) resistance to hydrolysis and absorption in the upper gastrointestinal tract, 2) fermentation by selective intestinal bacteria, and 3) enrichment of

beneficial bacterial species within the intestinal microbiota.[33] Only inulin and fructo-oligosaccharides, which together comprise the β2-1 fructans, have satisfied all three criteria; other oligosaccharides are considered candidate prebiotics.[33] Prebiotics have shown encouraging results in the stimulation of indigenous gastrointestinal bacteria, leading to a shift in the microbiota to a symbiotic state with multiple health benefits.[32, 33] In addition to positively influencing intestinal health, prebiotic supplementation has been used to selectively promote beneficial bacterial species within the oral microbiota.[34-36] Slomka and colleagues reported that supplementation with N-acetyl-D-mannosamine resulted in biofilm composition consisting of 97% beneficial species.[34] Clinical studies have demonstrated the effectiveness of prebiotics such as inulin to selectively enrich oral biofilms in species of the *Lactobacillus* and *Bifidobacterium* genera.[35, 37]

Although prior reports have demonstrated oral health benefits of *L. reuteri* and *B. animalis* subsp*. lactis,* the preferred probiotic species, the most effective vehicle of administration, and the optimal regimen remain unestablished. Moreover, prior research has not adequately characterized the value of combining probiotic and prebiotic supplementation. The current study aimed to evaluate the influence of *L. reuteri* or *B. animals* subsp. *lactis,* with and without prebiotic inulin, on microbial diversity and relative abundances of various bacterial species within dental biofilm cultures ex vivo.

MATERIALS AND METHODS

Ethical guidelines

This protocol utilized de-identified dental biofilm and saliva specimens and did not involve contact with patients or patient records. The Dwight David Eisenhower Army Medical Center Human Research Protections Office determined this research to be exempt from IRB review requirements (protocol #20-11301/931759), and the protocol was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013. Approval was granted to use de-identified specimens from the Fort Gordon Dental Health Activity Saliva and Dental Plaque Repository, which was reviewed and approved by the Naval Medical Center Portsmouth Institutional Review Board (protocol #20-10581/941839). Patients providing biofilm and saliva specimens for the repository provided written consent.

Inclusion and exclusion criteria

Three pairs of matched biofilm and saliva specimens were requested from the repository described above. The repository manager provided plaque and saliva from donors meeting the following criteria:

a) Periodontal diagnosis of Stage III or IV periodontitis
b) Radiographic alveolar bone loss and probing depth ≥ 6 mm at site of specimen collection
c) Age ≥ 18 years
d) Systemically healthy
e) Nonsmoker

f) No surgical or non-surgical periodontal therapy in the last 12 months

g) No antibiotic use in the last 12 months

Dental biofilm and saliva collection

Investigators included in the repository protocol collected dental biofilm specimens by inserting sterile coarse endodontic paper points[*] to the depth of the periodontal pocket of the first molar displaying the most severe periodontitis (Figure 1C). The paper point was moved laterally within the sulcus for 10 seconds and immediately placed into 1 mL of Amies transport medium[†] at 4°C. Unstimulated saliva was collected from the same donors and diluted ten-fold in reduced Ringers solution[‡]. Diluted saliva specimens were centrifuged at 1200 g × 10 min to remove large particulate matter then filter-sterilized through a membrane with 0.2-µm pores, divided into 2-mL aliquots, and stored at -20 °C.

Culture conditions

This study utilized a modification of the ex vivo biofilm model described by Velsko and Shaddox.[38] Hydroxyapatite (HA) disks,[§] 9.5 x 2 mm, were prepared for biofilm development by coating the disks in diluted sterile saliva for two hours at room temperature. The saliva was then removed and the disks were washed with 3 mL reduced Ringers solution. One washed disk was placed in each well of a 24-well plate,[‖] and 1 mL reduced sterile tryptic soy broth supplemented with 5 µg/mL hemin[¶] and 1 µg/mL menadione[#] (TSB-hm) was then gently added to each well. Gentle sonication of the biofilm specimens in a water bath for 30 seconds dispersed the plaque, and each well received 10 µL of a biofilm specimen from one of the three donors.

Broth cultures of *L. reuteri* (Strain designation 11284)[**] and *B. animalis* subsp*. lactis* (Strain designation IDCC 4301)[**] were grown to an optical density of 0.5 at 600 nm. These cultures were used to create 1/10 and 1/100 dilutions in reduced Ringer's solution. TSB-hm media was prepared and supplemented with inulin[††] to create final inulin concentrations of 0, 5, and 20 mg/mL.

A unique probiotic (*L. reuteri* or *B. animalis* subsp*. lactis*; control, undiluted, 1/10 dilution, or 1/100 dilution) and prebiotic (0, 5, or 20 mg/mL) combination was added to each well, producing a total of 21 experimental conditions (Figure 1A). Each well received 10 µL of the indicated probiotic culture and 1 mL of TSB-hm media with or without inulin supplementation. Well plates were then placed in an anaerobic incubator[‡‡] at 37°C-75% N_2/10% CO_2/10% H_2 for static growth.

Every 48 hours all media was gently removed from each well and 1 mL of fresh media with or without inulin was added. On the eighth day, new saliva-coated and washed HA disks were added to fresh wells. The HA disk with mature biofilm (eighth day of growth) from each of the 21 wells for each of the three donors was removed from the well and added to 1 mL reduced Ringer's solution. The disks were sonicated in an ice water bath for 30 seconds, vortexed briefly to disperse any remaining deposits, and 50 µL of the suspension was used to inoculate the appropriate well for the next generation. This procedure was repeated for 10 total generations (80 days of bacterial growth) for each of the three biofilm specimens. The residual biofilm suspensions not used to inoculate the next generation were used for DNA extraction (Figure 1B).

Viable cell count estimations

The biofilm and probiotic suspensions used to inoculate the first generation for each biofilm specimen were plated to estimate viable cell counts. Tryptic soy agar with hemin and menadione, *Lactobacillus* MRS agar,[§§] and *Bifidobacterium* selective agar[‖‖] were used to plate serial dilutions of the biofilm specimens, *L. reuteri* cultures, and *B. animalis* subsp*. lactis* cultures*,* respectively. The plates were incubated at 37°C-75% N_2/10% CO_2/10% H_2 and read after 72 hours of growth.

Differential species abundance determination (human oral microbiome identification)

The residual biofilm suspensions from generations 1, 2, 3, 4, 6, 8, and 10 (days 8, 16, 24, 32, 48, 64, and 80, respectively) were centrifuged at 10,000 rpm for 2 min to pellet cells, and the supernatant discarded. The pelleted cells were stored at -20°C for DNA extraction. DNA was extracted from the biofilm pellets of interest and submitted to a commercial lab[¶¶] for human oral microbiome analyses via 16S rRNA sequencing.[##] This system is capable of identifying over 600 genera. Of these, 19 genera have been associated with periodontitis.[39, 40] The influence of probiotic inoculation and prebiotic supplementation on the relative abundance of 19 periodontitis-associated genera was recorded, and seven genera were selected for the statistical analyses described below.

Relative abundance analyses

Genus-level relative abundance analyses were completed at the donor and study population levels. Hierarchical multiple regression models were conducted using Statistical

Package for the Social Sciences[***] to determine if the addition of inulin or probiotic strains influenced the relative abundance of seven selected genera over the ten generations observed. The full models consisted of growth time, concentration of *B. animalis* or *L. reuteri* inoculation, and concentration of supplemental inulin. Independent samples t-tests were used to compare mean relative abundance values in experimental versus control cultures for each genera of interest. Statistical significance was assessed at an alpha level of 0.05.

Community diversity analyses

All community diversity analyses were completed at the study population level using an open-source next-generation microbiome bioinformatics platform.[†††, 41] Intra-group diversity (alpha diversity) was assessed using the metrics observed operational taxonomic units (OTUs) and Faith's phylogenetic diversity (FPD) on tables rarefied to a depth of 35,300 reads/sample. Rarefications were performed and alpha diversity metrics calculated 10 times and then averaged. Differences in alpha diversity between experimental groups were evaluated using the Kruskal–Wallis *H* test. Statistical significance was assessed at an alpha level of 0.05. Inter-group diversity (beta diversity) was assessed using weighted UniFrac distance. Principal coordinates analysis was performed on beta diversity metrics, and the results were plotted on three axes.

RESULTS

At eight days of growth, biofilms of adequate mass for DNA extraction/purification and establishment of subsequent generations were present in all inoculated wells. Extraction and purification of DNA from all samples yielded sufficient quantity and quality for microbial identification and relative abundance analysis via 16S rRNA sequencing.

Figure 2 presents study population-level changes in relative abundance values for the 19 periodontitis-associated genera over ten generations of ex vivo biofilm growth. As expected, relative abundance values remained stable in cultures receiving no probiotic or prebiotic supplementation. The relative abundance of *Lactobacillus* and *Bifidobacterium* species increased and putative periodontal pathogens decreased in cultures receiving inulin supplementation versus cultures not receiving inulin.

In relative abundance analysis (Figure 3), addition of either probiotic strain alone (no inulin supplementation) produced no statistically significant change for any genera of interest. Among cultures receiving only inulin supplementation (no probiotic inoculation), each genera of interest exhibited statistically significant changes in mean relative abundance values, with *Streptococcus, Veillonella, Fusobacterium, Parvimonas,* and *Prevotella* species decreasing in relative abundance and native *Bifidobacterium* and *Lactobacillus* species increasing in relative abundance. In cultures inoculated with either probiotic strain, inulin supplementation produced statistically significant changes in mean relative abundance for each genera of interest similar to the effects noted in cultures receiving inulin alone. For some genera, the effect of inulin supplementation appeared dose dependent.

Donor-level and study population-level results of the hierarchical multiple regression analyses are presented in Tables 1 and 2, respectively. At the donor-level and study population-level, inulin supplementation led to statistically significant increases in mean relative abundance values of *Lactobacillus* and *Bifidobacterium* species ($p<0.001$). Furthermore, inulin supplementation resulted in statistically significant ($p<0.001$) decreases in *Streptococcus, Veillonella, Fusobacterium, Parvimonas,* and *Prevotella* species. Inoculation with *L. reuteri* led to a statistically significant increase in *Lactobacillus* species only ($p<0.05$); likewise, inoculation with *B. animalis* subsp. *lactis* produced a statistically significant increase in *Bifidobacterium* species only ($p<0.05$). Inoculation with either *L. reuteri* or *B. animalis* subsp. *lactis* produced no statistically significant change in the relative abundances of the pathogenic genera evaluated.

Figure 4 presents the study population-level diversity analyses completed in QIIME 2. In alpha analyses by observed OTUs and FPD, inulin supplementation at 20 mg/ml with or without *L. reuteri* or *B. animalis* subsp. *lactis* inoculation led to statistically significant reduction in alpha diversity ($p<0.001$). Beta diversity across experimental groups also appears altered with a distinct change in community profile between control conditions and biofilms receiving inulin supplementation at 20 mg/ml with or without *L. reuteri* or *B. animalis* subsp. *lactis* inoculation; control conditions clustered separately from inulin treated biofilms.

DISCUSSION

The purpose of this investigation was to assess the influence of two probiotic bacterial strains, alone and in combination with a prebiotic, on biodiversity within human dental biofilm cultures ex vivo. Outcome measures recorded in this investigation included two distinct diversity indices. Alpha diversity indices reflect the richness (number of unique taxa) and evenness (similarity in relative abundance values of the taxa present) within a microbial community, whereas beta diversity scores permit comparison of the overall dissimilarity in community structure across samples.[8] Other dimensions of microbial ecology include relative abundance (percentage of the total microbes in a community represented by a particular microbe), abundance (absolute quantity of a microbe within a sample), and prevalence (mere presence of a particular microbe within a sample).[8] In addition, the abundance ratio of two taxa can provide practical insight. For example, in gut microbial ecology, the *Bacteroidetes*:*Firmicutes* ratio has been proposed as a relevant biomarker.[5]

Probiotic and prebiotic applications in the prevention and treatment of inflammatory disease represent areas of intense research focus in recent years.[12-14, 17-37, 42] Within the gut, prebiotics/metabolites stimulate mucin production due to intraluminal pH reduction, disfavor colonization of some pathogens by acidifying the local environment, bind specific G protein coupled receptors on immune cell surfaces, and modulate gene expression in epithelial cells.[33] Researchers have associated prebiotic supplementation with positive effects on both mucosal and systemic immune function.[33] Likewise, in the oral cavity probiotic supplementation may favorably alter the microbiome and dampen the ensuing host immune response,[17-30, 35, 36] and

supplemental prebiotics may enhance the clinical benefit predominantly by enriching the microbiota in beneficial bacterial strains.[32-35, 37]

To our knowledge, no prior study has evaluated the influence of prebiotic inulin on dental plaque specimens from periodontitis patients ex vivo. Under the described conditions, initial supplementation with probiotic *L. reuteri* or *B. animalis* subsp. *lactis* produced no significant alteration of the biofilm composition in terms of pathogen abundance or overall diversity. In contrast, inulin supplementation alone led to dose-dependent increases in health-associated genera and decreases in pathogenic genera. Inulin supplementation also significantly decreased the alpha diversity of the microbiota, as assessed by observed OTUs and FPD. Abusleme and colleagues compared microbial diversity under conditions of health versus periodontitis using 16S rRNA sequencing and reported higher diversity and greater biomass in the periodontitis cohort.[40] Thus, our observation of reduced microbial diversity among cultures receiving inulin may imply a shift toward a healthy microbiota.

Caution is prudent in the interpretation of our results. Cultures evaluated in this study derived from only three human donors. Moreover, although investigators have made substantial progress in understanding oral microbial profiles differentiating health and disease,[9, 10, 40] alpha diversity per se has not been validated as a reliable marker. Indeed, considering the unique microbial ecosystems across the various body regions, it appears necessary to interpret the significance of microbial diversity in context. Reduction in biodiversity is not universally favorable. It is accepted that community stability and high species diversity in the gut are attributes of a healthy microbiota, with exogenous variables

such as exercise, diet, and probiotic/prebiotic supplementation influencing the structure of gut communities.[42-44] Likewise, complex microbiota have been observed in maxillary sinuses of patients with and without chronic sinusitis; however, microbial communities in inflamed sinuses typically exhibit reduced diversity.[7] In contrast, molecular analysis of microbiota associated with bacterial vaginosis suggests dramatic increases in bacterial abundance and diversity compared with healthy controls.[45] Intraorally, reports identifying the biodiversity of microbiota at dental caries sites are conflicted.[46] Although some studies have found increased microbial complexity at caries-affected sites, low pH can select for acid-tolerant species, leading to a less diverse and more extreme microflora.[46] Biofilms at the dentogingival interface are among the most complex in the human body.[8,9,40] Interpreting observed biodiversity in such communities remains an area of investigation in periodontics. Eubiosis—a functional balance within the microbial ecosystem—has been characterized by diversity of species, ability to withstand perturbation (resistance), ability to return to baseline after removal of a stressful stimulus (resilience), and stability between the microbial community and the host.[9] Nevertheless, at least one study has reported higher diversity in periodontitis compared with control samples.[40]

Inulin supplementation purportedly produces beneficial effects by selecting for health-associated inulin-fermenting species. [32-35, 37] Degradation of inulin—a long, water-soluble polymer—produces smaller fructans, which neighboring species may metabolize.[47] In research involving the gut microbiota of humans and feed animals, this interspecies cross-feeding has been found to promote gastrointestinal health.[48, 49] It is possible that observations in the

present ex vivo oral biofilm study reflect a combination of direct promotion of inulin-fermenting bacteria and cross feeding of secondary consumers in similar and distant genera.

Results of the present investigation are consistent with findings from previous studies reporting prebiotic effects on oral microbiome composition. In an in vitro biofilm model consisting of only 14 oral bacterial species, Slomka and colleagues reported that three prebiotic substrates successfully increased the beneficial proportion of genera to > 95%.[34] While this study did not evaluate inulin as a prebiotic, the authors did assess similar long-chain, water-soluble polysaccharides that exhibit degradation comparable to that of inulin.[34] In a randomized controlled trial, Mousquer and colleagues used a combination of inulin and *Lactobaciullus salivarius* for the treatment of halitosis.[50] This combination resulted in a significant decrease in oral malodor compared to placebo suggesting a modification of the microbiome, although microbiological analysis was limited in this study.[50] No prior study has evaluated the effect of inulin in combination with a probiotic strain in the treatment of periodontitis or maintenance of periodontal health.

The ex vivo model utilized in the present study appears appropriate for evaluating prebiotics, probiotics, and prebiotic/probiotic combinations. The composition of control cultures remained consistent over ten generations of biofilm growth in the present study, as expected. For many genera of interest, the effect induced by each experimental condition versus control was evident by the earliest time point evaluated. Having validated our methods, future studies involving larger sample sizes and more powerful statistical analyses are necessary to confirm observations in this initial investigation. One limitation of the described model is

that no data were generated prior to the eighth day of growth in the first biofilm generation. Another potential limitation of this study is in the use of relative abundance values. While this quantifier permits comparisons in biofilm composition, it provides no information on absolute CFU counts for the genera of interest. In this study, large increases in relative abundances of *Lactobacillus* and *Bifidobacterium* species were observed in the presence of inulin. However, the actual counts of the pathogenic genera may have decreased, remained stable, or even increased.

Based on our findings, prebiotics appear to be promising adjuncts in the prevention and treatment of periodontal disease through the modulation of the subgingival biofilm. Although in vitro culture methods allow for sustained contact between the biofilm and supplemented media, in vivo applications of inulin to subgingival biofilms with prolonged contact time will be a challenging therapeutic obstacle. Additional study further elucidating the underlying biologic rationale and optimal mechanism of administration through controlled clinical research are warranted.

CONCLUSIONS

In conclusion, we have demonstrated a dose-dependent decrease in the relative abundance values of select periodontal pathogens accompanied by a dose-dependent increase in the probiotic genera *Lactobacillus* and *Bifidobacterium* in response to continued inulin supplementation. These results suggest that prebiotic supplementation may represent a viable strategy for promotion of periodontal health through favorable modification of the oral microbiome.

AUTHOR CONTRIBUTIONS

Conception and design of the study: AC, JA, DB, TJ. Acquisition, analysis, or interpretation of data: AC, DB, JD. Drafting the work or revising it critically for important intellectual content: AC, TJ, DB, BS, AL, JA. Final approval of the version to be published: all authors.

ACKNOWLEDGEMENTS

The authors report no conflicts of interest related to this report. The views expressed in this manuscript are those of the authors and do not necessarily reflect the official policy of the Department of Defense, Department of Army, U.S. Army Medical Department, or Uniformed Services University of the Health Sciences.

[*]Dentsply; York, PA

[†]Puritan; Guilford, Maine

[‡]Millipore; Burlington, MA

[§]Clarkson Chromatography; South Williamsport, PA

[‖]Neogen; Lansing, MI

[¶]Thermo Scientific; Waltham, MA

[#]Sigma; St. Louis, MO

[**]ATCC; Manassas, Virgina

[††]Thermo Scientific; Waltham, MA

[‡‡]Bactron 600-2; MRC Laboratory Instruments; London, UK

[§§]BD Difco; Fischer Scientific; Waltham, MA

[|||]BIFIDO; Anaerobe Systems; Morgan Hill, CA

[¶¶]CD Genomics, Shirley, NY

[##]MiSeq System, Illumina, San Diego, CA

[***]IBM SPSS for Windows, v.27, SPSS Inc., Chicago, IL

[†††]Quantitative Insights Into Microbial Ecology-2, QIIME 2

REFERENCES

1. Gilbert JA, Blaser MJ, Caporaso JG, Jansson JK, Lynch SV, Knight R. Current understanding of the human microbiome. *Nat Med* 2018;24:392-400.

2. Sender R, Fuchs S, Milo R. Are we really vastly outnumbered? Revisiting the ratio of bacterial to host cells in humans. *Cell* 2016;164:337-340.

3. Qin J, Li R, Raes J, Arumugam M, et al. A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* 2010;464:59–65.

4. Turnbaugh PJ, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. The human microbiome project. *Nature* 2007;449:804-810.

5. Bamola VD, Ghosh A, Kapardar RK, et al. Gut microbial diversity in health and disease: experience of healthy Indian subjects, and colon carcinoma and inflammatory bowel disease patients. *Microb Ecol Health Dis* 2017;28:1322447. doi: 10.1080/16512235.2017.1322447.

6. Kostic AD, Chun E, Robertson L, et al. Fusobacterium nucleatum potentiates intestinal tumorigenesis and modulates the tumor-immune microenvironment. *Cell Host Microbe* 2013;14:207-215.

7. Lee JT, Frank DN, Ramakrishnan V. Microbiome of the paranasal sinuses: update and literature review. *Am J Rhinol Allergy* 2016;30:3-16.

8. Scannapieco FA, Dongari-Bagtzoglou A. Dysbiosis revisited: Understanding the role of the oral microbiome in the pathogenesis of gingivitis and periodontitis: A critical assessment. *J Periodontol* 2021;92:1071-1078.

9. Kumar PS. Microbial dysbiosis: The root cause of periodontal disease. *J Periodontol* 2021;92:1079-1087.

10. Kragen H. The treatment of inflammatory affections of the oral mucosa with a lactic acid bacterial culture preparation. *Zahnarztl Welt* 1954;9:306-308.

11. Lilly DM, Stillwell RH. Probiotics: growth-promoting factors produced by microorganisms. *Science* 1965;147:747-748.

12. Reid G, Gadir AA, Dhir R. Probiotics: reiterating what they are and what they are not. *Front Microbiol* 2019;10:424.

13. Matsubara VH, Bandara HM, Ishikawa KH, Mayer MP, Samaranayake LP. The role of probiotic bacteria in managing periodontal disease: a systematic review. *Expert Rev Anti Infect Ther* 2016;14:643-655.

14. Kuru BE, Laleman I, Yalnizoglu T, Kuru L, Teughels W. The influence of a Bifidobacterium animalis probiotic on gingival health: a randomized controlled clinical trial. *J Periodontol* 2017;88:1115-1123.

15. Michalowicz BS, Diehl SR, Gunsolley JC, et al. Evidence of a substantial genetic basis for risk of adult periodontitis. *J Periodontol* 2000;71:1699-1707.

16. Ezzo PJ, Cutler CW. Microorganisms as risk indicators for periodontal disease. *Periodontol 2000* 2003;32:24-35.

17. Teughels W, Loozen G, Quirynen M. Do probiotics offer opportunities to manipulate the periodontal oral microbiota? *J Clin Periodontol* 2011;38 Suppl 11:159-177.

18. Ince G, Gursoy H, Ipci SD, Cakar G, Emekli-Alturfan E, Yilmaz S. Clinical and biochemical evaluation of lozenges containing Lactobacillus reuteri as an adjunct to non-surgical periodontal therapy in chronic periodontitis. *J Periodontol* 2015;86:746-754.

19. Teughels W, Durukan A, Ozcelik O, Pauwels M, Quirynen M, Haytac MC. Clinical and microbiological effects of Lactobacillus reuteri probiotics in the treatment of chronic periodontitis: a randomized placebo-controlled study. *J Clin Periodontol* 2013;40:1025-1035.

20. Romani Vestman N, Chen T, Lif Holgerson P, Ohman C, Johansson I. Oral microbiota shift after 12-week supplementation with Lactobacillus reuteri DSM 17938 and PTA 5289; a randomized control trial. *PLoS One* 2015;10:e0125812.

21. Tekce M, Ince G, Gursoy H, et al. Clinical and microbiological effects of probiotic lozenges in the treatment of chronic periodontitis: a 1-year follow-up study. *J Clin Periodontol* 2015;42:363-372.

22. Schlagenhauf U, Rehder J, Gelbrich G, Jockel-Schneider Y. Consumption of Lactobacillus reuteri-containing lozenges improves periodontal health in navy sailors at sea: A randomized controlled trial. *J Periodontol* 2020;91:1328-1338.

23. Ricoldi MST, Furlaneto FAC, Oliveira LFF, et al. Effects of the probiotic Bifidobacterium animalis subsp. lactis on the non-surgical treatment of periodontitis. A histomorphometric, microtomographic and immunohistochemical study in rats. *PLoS One* 2017;12:e0179946.

24. Oliveira LF, Salvador SL, Silva PH, et al. Benefits of Bifidobacterium animalis subsp. lactis probiotic in experimental periodontitis. *J Periodontol* 2017;88:197-208.

25. Toiviainen A, Jalasvuori H, Lahti E, et al. Impact of orally administered lozenges with Lactobacillus rhamnosus GG and Bifidobacterium animalis subsp. lactis BB-12 on the number of salivary mutans streptococci, amount of plaque, gingival inflammation and the oral microbiome in healthy adults. *Clin Oral Investig* 2015;19:77-83.

26. Invernici MM, Salvador SL, Silva PHF, et al. Effects of Bifidobacterium probiotic on the treatment of chronic periodontitis: A randomized clinical trial. *J Clin Periodontol* 2018;45:1198-1210.

27. Invernici MM, Furlaneto FAC, Salvador SL, et al. Bifidobacterium animalis subsp lactis HN019 presents antimicrobial potential against periodontopathogens and modulates the immunological response of oral mucosa in periodontitis patients. *PLoS One* 2020;15:e0238425.

28. Allaker RP, Stephen AS. Use of probiotics and oral health. *Curr Oral Health Rep* 2017;4:309-318.

29. Dassi E, Ferretti P, Covello G, et al. The short-term impact of probiotic consumption on the oral cavity microbiome. *Sci Rep* 2018;8:10476.

30. Armitage GC. A brief history of periodontics in the United States of America: Pioneers and thought-leaders of the past, and current challenges. *Periodontol 2000* 2020;82:12-25.

31. Ma D, Forsythe P, Bienenstock J. Live Lactobacillus rhamnosus [corrected] is essential for the inhibitory effect on tumor necrosis factor alpha-induced interleukin-8 expression. *Infect Immun* 2004;72:5308-5314.

32. Roberfroid M. Prebiotics: the concept revisited. *J Nutr* 2007;137:830S-837S.

33. Lomax AR, Calder PC. Prebiotics, immune function, infection and inflammation: a review of the evidence. *Br J Nutr* 2008;101:633-658.

34. Slomka V, Herrero ER, Boon N, et al. Oral prebiotics and the influence of environmental conditions in vitro. *J Periodontol* 2018;89:708-717.

35. Slomka V, Hernandez-Sanabria E, Herrero ER, et al. Nutritional stimulation of commensal oral bacteria suppresses pathogens: the prebiotic concept. *J Clin Periodontol* 2017;44:344-352.

36. Nguyen T, Brody H, Radaic A, Kapila Y. Probiotics for periodontal health-Current molecular findings. *Periodontol 2000* 2021;87:254-267.

37. Kolida S, Tuohy K, Gibson GR. Prebiotic effects of inulin and oligofructose. *Br J Nutr* 2002;87 Suppl 2:S193-197.

38. Velsko IM, Shaddox LM. Consistent and reproducible long-term in vitro growth of health and disease-associated oral subgingival biofilms. *BMC Microbiol* 2018;18:70.

39. Socransky SS, Haffajee AD, Cugini MA, Smith C, Kent RL, Jr. Microbial complexes in subgingival plaque. *J Clin Periodontol* 1998;25:134-144.

40. Abusleme L, Dupuy AK, Dutzan N, et al. The subgingival microbiome in health and periodontitis and its relationship with community biomass and inflammation. *ISME J* 2013;7:1016-1025.

41. Bolyen E, Rideout JR, Dillon MR, et al. Reproducible, interactive, scalable and extensible microbiome data science using QIIME 2. *Nat Biotechnol* 2019;37:852-857.

42. Mengheri E. Health, probiotics, and inflammation. *J Clin Gastroenterol* 2008;42 Suppl 3 Pt 2:S177-178.

43. Campbell SC, Wisniewski PJ. Exercise is a novel promoter of intestinal health and microbial diversity. *Exerc Sport Sci Rev* 2017;45:41-47.

44. Bamola VD, Ghosh A, Kapardar RK, et al. Gut microbial diversity in health and disease: experience of healthy Indian subjects, and colon carcinoma and inflammatory bowel disease patients. *Microb Ecol Health Dis* 2017;28:1322447. doi: 10.1080/16512235.2017.1322447.

45. Ling Z, Kong J, Liu F, Zhu H, Chen X, Wang Y, Li L, Nelson KE, Xia Y, Xiang C. Molecular analysis of the diversity of vaginal microbiota associated with bacterial vaginosis. *BMC Genom* 2010;11:1-6.

46. Marsh PD. Microbiology of dental plaque biofilms and their role in oral health and caries. *Dent Clin N Am* 2010;54:441-454.

47. Rakoff-Nahoum S, Foster KR, Comstock LE. The evolution of cooperation within the gut microbiota. *Nature* 2016;533:255-259.

48. Vandeputte D, Falony G, Vieira-Silva S, et al. Prebiotic inulin-type fructans induce specific changes in the human gut microbiota. *Gut* 2017;66:1968-1974.

49. Zhu Y, Liu J, Lopez JM, Mills DA. Inulin fermentation by Lactobacilli and Bifidobacteria from dairy calves. *Appl Environ Microbiol* 2020;87.

50. Mousquer CR, Della Bona A, Milani DC, et al. Are Lactobacillus salivarius G60 and inulin more efficacious to treat patients with oral halitosis and tongue coating than the probiotic alone and placebo? A randomized clinical trial. *J Periodontol* 2020;91:775-783.

FIGURES

A

Condition	Inulin mg/mL	Probiotic dilutions	
		L. reuteri (OD_{600} 0.5)	*B. animalis* (OD_{600} 0.5)
1	0	--	--
2	5	--	--
3	20	--	--
4	0	1/100	--
5	5	1/100	--
6	20	1/100	--
7	0	1/10	--
8	5	1/10	--
9	20	1/10	--
10	0	1/1	--
11	5	1/1	--
12	20	1/1	--
13	0	--	1/100
14	5	--	1/100
15	20	--	1/100
16	0	--	1/10
17	5	--	1/10
18	20	--	1/10
19	0	--	1/1
20	5	--	1/1
21	20	--	1/1

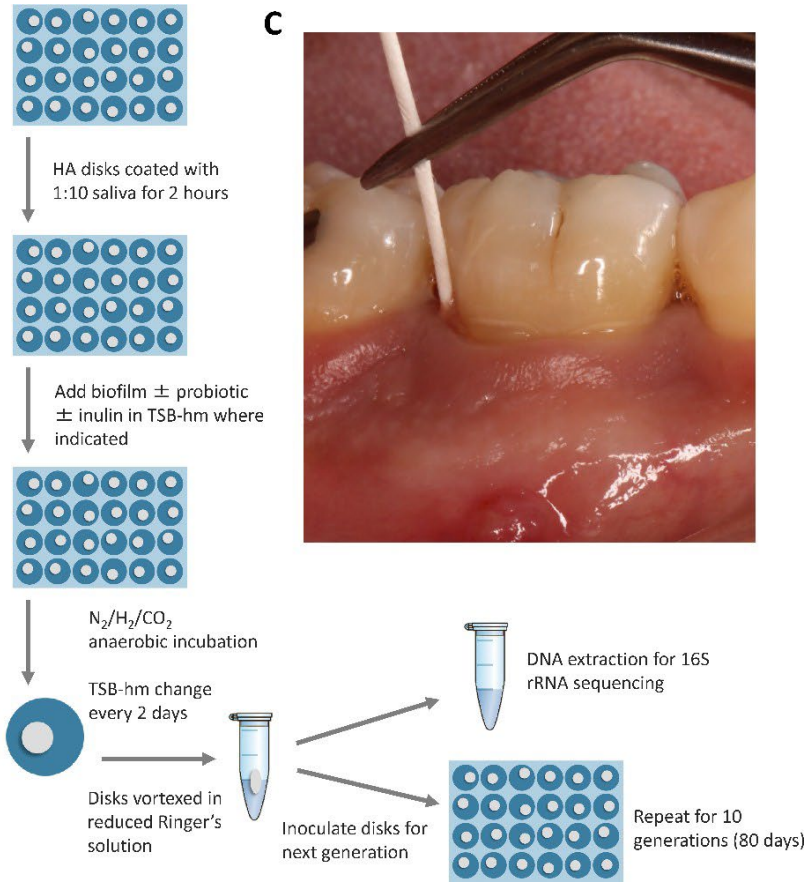


FIGURE 1. Experimental methods. **A)** Experimental conditions applied to each donor biofilm. **B)** Biofilm development schematic utilizing 24-well plates containing hydroxyapatite disks. All ex vivo biofilm growth completed in anaerobic chamber at 37°C-75% N_2/10% CO_2/10% H_2. **C)** Demonstration of the biofilm collection technique. Dental biofilm and saliva were requested from a repository of de-identified specimens. Donors had received stage III or IV periodontitis diagnoses, and the investigator collected biofilm using a sterile paper point at the first molar site exhibiting greatest bone/attachment loss.

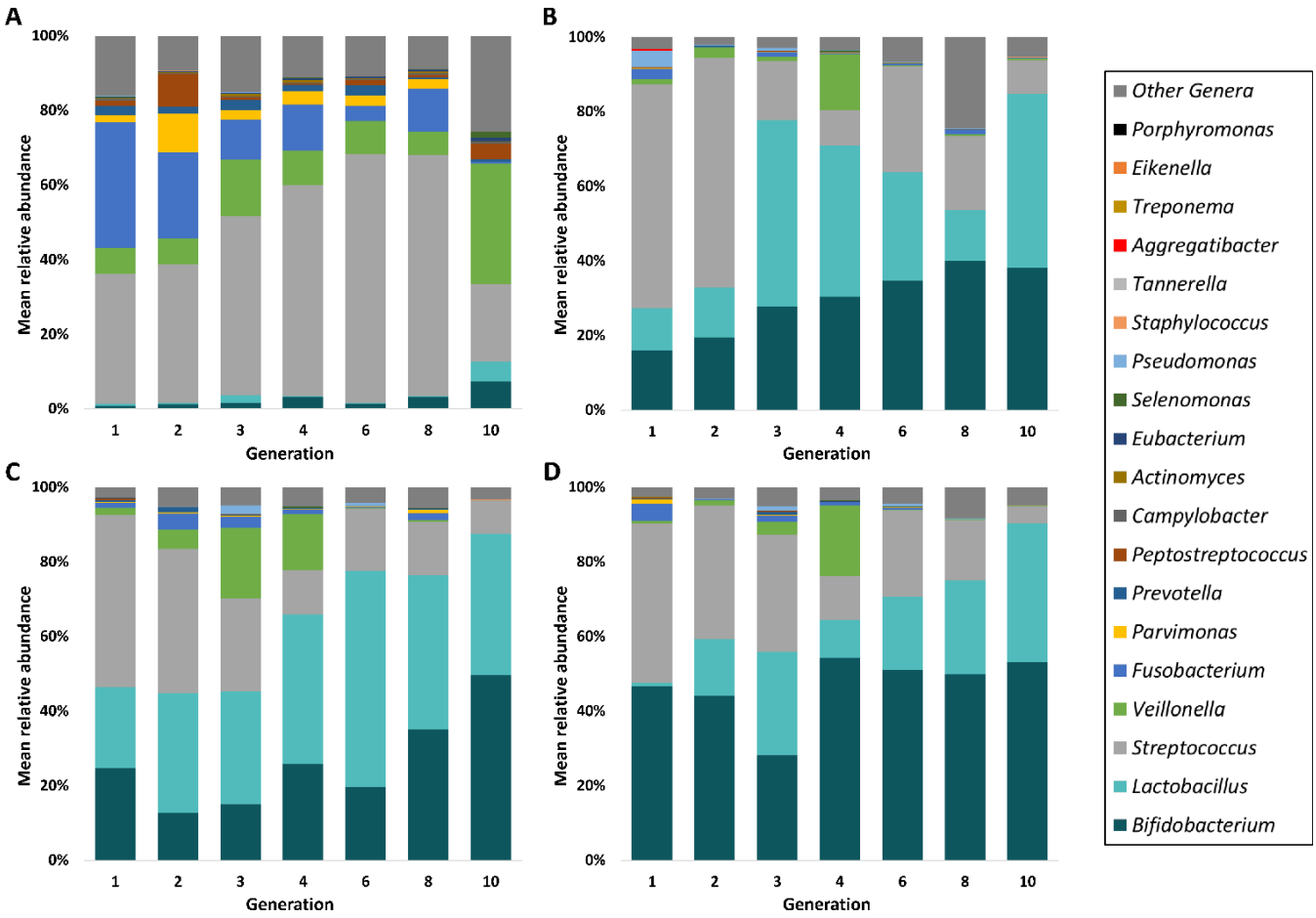


Figure 2. Mean relative abundance of 19 genera at each generation of ex vivo growth. **A**) Control biofilms not inoculated with probiotic or supplemented with inulin showed minimal change in abundance of pathogenic species or naturally occurring probiotic species. **B**) Cultures supplemented with 20 mg/ml inulin exhibited increased relative abundance of native *Lactobacillus* and *Bifidobacterium* species as well as decreased relative abundance of pathogenic genera. **C**) *L. reuteri* inoculation plus 20 mg/ml supplemental inulin led to a greater increase in *Lactobacillus* species compared with inulin supplementation alone. **D**) *B. animalis* inoculation plus 20 mg/ml supplemental inulin led to a greater increase in *Bifidobacterium* species compared to inulin supplementation alone.

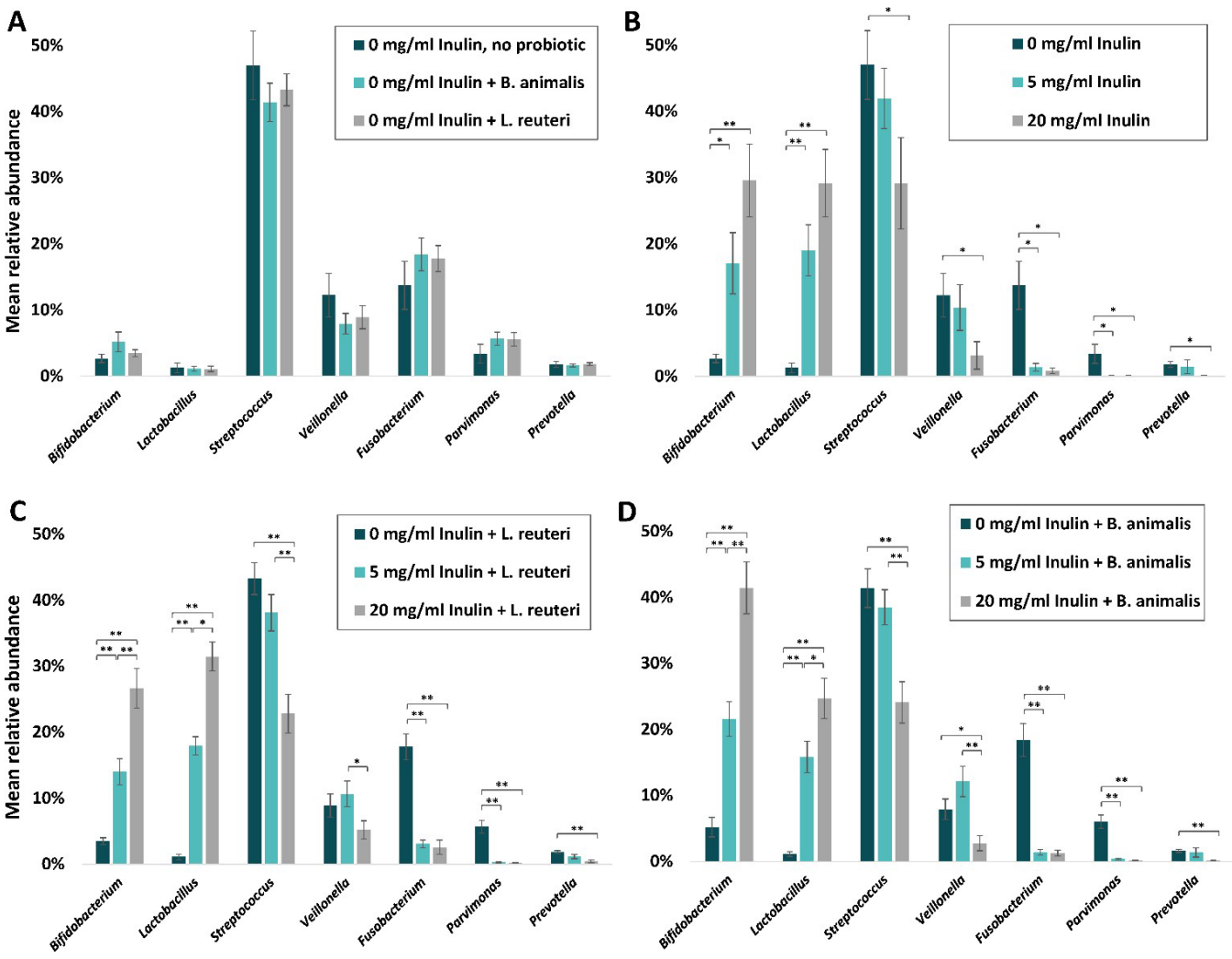
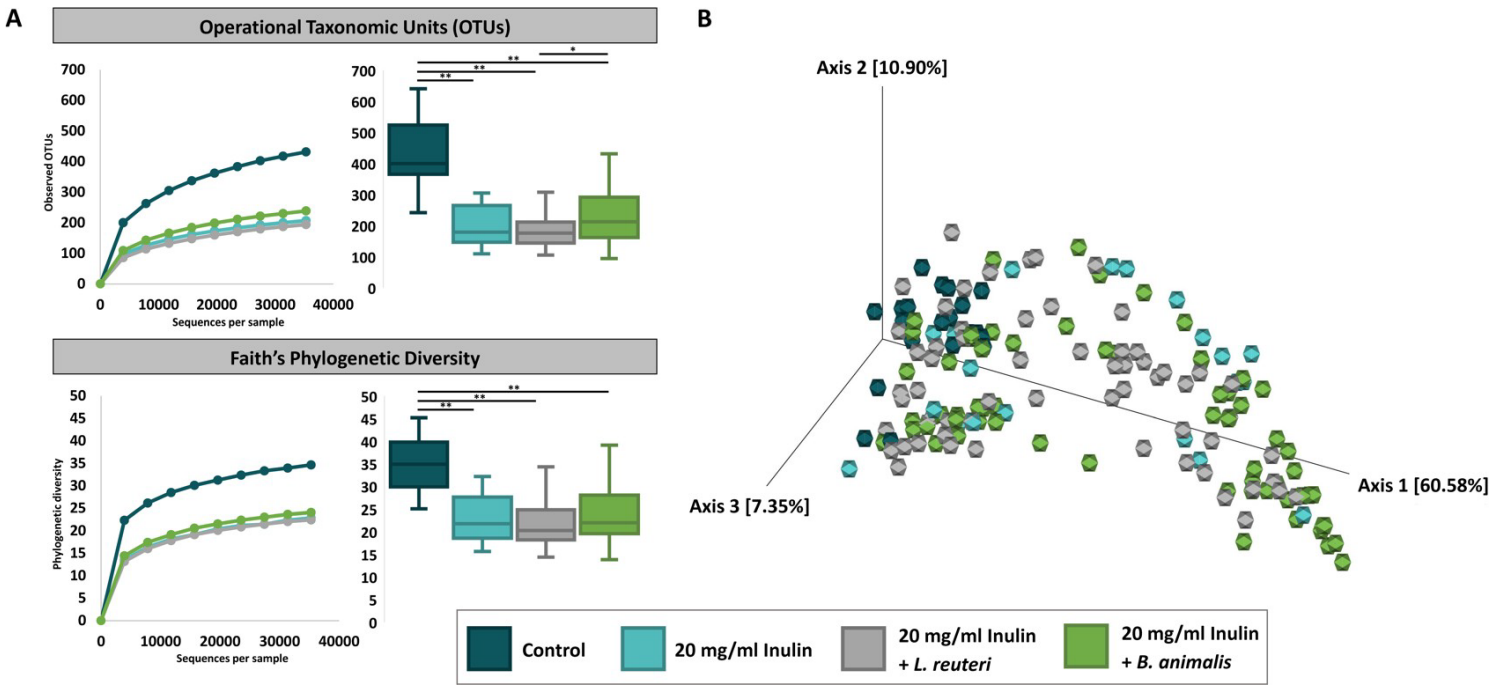


Figure 3. Mean relative abundance values across 10 generations of ex vivo growth. $^{**}p<0.001$, $^{*}p<0.05$. **A**) Varying initial probiotic inoculation with no prebiotic inulin produced no statistically significant changes in relative abundance of any evaluated genera. **B**) Prebiotic inulin supplementation with no initial probiotic inoculation led to significant increases in relative abundance of native *Bifidobacterium* and *Lactobacillus* species as well as significant decreases in pathogenic genera. **C**) *L. reuteri* inoculation plus inulin supplementation and inulin supplementation alone led to led to significant increases in relative abundance of native

Bifidobacterium and *Lactobacillus* species as well as significant decreases in pathogenic genera. **D**) *B. animalis* inoculation plus inulin supplementation and inulin supplementation alone led to significant increases in relative abundance of native *Bifidobacterium* and *Lactobacillus* species as well as significant decreases in pathogenic genera.



** p<0.001, * p<0.05

Figure 4. Ex vivo plaque biofilm diversity analysis. **A**) Alpha diversity. All cultures receiving prebiotic inulin exhibited reduction in alpha diversity, as assessed by recorded operational taxonomic unit counts (top) and Faith's phylogenetic diversity (bottom). **B**) Beta diversity. In weighted UniFrac distance analysis, control and inulin-treated cultures clustered separately.

TABLES

Genus	Variables added to model	Donor 1 Coef.	Donor 1 95% CI Lower Bound	Donor 1 95% CI Upper Bound	Donor 1 R^2	Donor 2 Coef.	Donor 2 95% CI Lower Bound	Donor 2 95% CI Upper Bound	Donor 2 R^2	Donor 3 Coef.	Donor 3 95% CI Lower Bound	Donor 3 95% CI Upper Bound	Donor 3 R^2
Bifidobacterium	Conc. of *B. animalis*	0.093	0.047	0.140	0.108	***0.087**	0.003	0.172	0.035	***0.090**	0.003	0.177	0.147
	Conc. of *L. reuteri*	-0.002	-0.049	0.044	0.108	-0.084	-0.169	0.000	0.046	-0.020	-0.107	0.067	0.148
	Conc. of Inulin	***0.002**	0.001	0.004	0.147	****0.024**	0.021	0.027	0.602	****0.015**	0.011	0.018	0.432
Lactobacillus	Conc. of *B. animalis*	-0.003	-0.107	0.101	0.133	-0.042	-0.103	0.019	0.028	***-0.073**	-0.132	-0.014	0.041
	Conc. of *L. reuteri*	***0.111**	0.007	0.215	0.133	0.056	-0.005	0.117	0.020	0.023	-0.036	0.081	0.010
	Conc. of Inulin	****0.018**	0.014	0.022	0.426	****0.012**	0.009	0.014	0.410	****0.008**	0.006	0.011	0.287
Streptococcus	Conc. of *B. animalis*	-0.083	-0.175	0.009	0.020	-0.087	-0.176	0.002	0.037	-0.010	-0.119	0.098	0.239
	Conc. of *L. reuteri*	-0.034	-0.127	0.058	0.024	-0.022	-0.112	0.067	0.038	-0.072	-0.180	0.036	0.247
	Conc. of Inulin	-0.002	-0.006	0.002	0.032	****-0.020**	-0.024	-0.017	0.498	***-0.006**	-0.010	-0.002	0.284
Veillonella	Conc. of *B. animalis*	-0.008	-0.083	0.067	0.055	***0.073**	0.021	0.125	0.129	-0.006	-0.068	0.055	0.034
	Conc. of *L. reuteri*	-0.039	-0.114	0.036	0.062	0.012	-0.041	0.064	0.130	0.048	-0.014	0.109	0.049
	Conc. of Inulin	-0.001	-0.004	0.002	0.067	***-0.004**	-0.006	-0.002	0.218	***-0.004**	-0.006	-0.001	0.111
Fusobacterium	Conc. of *B. animalis*	0.000	-0.076	0.076	0.094	0.004	-0.034	0.042	0.080	-0.015	-0.050	0.019	0.057
	Conc. of *L. reuteri*	-0.035	-0.111	0.042	0.098	***0.043**	0.004	0.081	0.105	0.240	-0.011	0.058	0.067
	Conc. of Inulin	****-0.010**	-0.013	-0.007	0.301	****-0.004**	-0.006	-0.003	0.256	****-0.004**	-0.006	-0.003	0.265
Parvimonas	Conc. of *B. animalis*	***0.022**	0.001	0.043	0.032	-0.016	-0.043	0.012	0.044	0.009	-0.009	0.027	0.029
	Conc. of *L. reuteri*	-0.010	-0.031	0.012	0.037	0.000	-0.028	0.027	0.044	0.016	-0.002	0.035	0.048
	Conc. of Inulin	****-0.002**	-0.003	-0.001	0.148	****-0.003**	-0.004	-0.002	0.210	****-0.001**	-0.002	-0.001	0.137
Prevotella	Conc. of *B. animalis*	-0.002	-0.007	0.004	0.088	0.003	-0.003	0.009	0.013	0.001	-0.020	0.022	0.061
	Conc. of *L. reuteri*	0.000	-0.005	0.006	0.088	0.003	-0.003	0.009	0.021	0.002	-0.019	0.023	0.061
	Conc. of Inulin	****-0.001**	-0.001	0.000	0.271	****-0.003**	-0.001	0.000	0.121	****-0.001**	-0.002	0.000	0.100

Table 1. Donor-level hierarchical multiple regression analysis. Effect of probiotic and prebiotic supplementation on relative abundance predictive values. *$p < 0.05$, **$p < 0.001$. Coef. values represent the predicted change in genus relative abundance per unit change in variable added to model. Concentrations (Conc.) of *B. animalis* and *L. reuteri* calculated as dilutions of initial broth culture with OD of 0.5. Concentration (Conc.) of inulin calculated as mg/ml.

Genus	Variables added to model	Combined	95% Confidence Interval		R^2
		Coef.	Lower Bound	Upper Bound	
Bifidobacterium	Conc. of *B. animalis*	***0.090**	0.035	0.146	0.027
	Conc. of *L. reuteri*	-0.035	-0.091	0.020	0.030
	Conc. of Inulin	****0.014**	0.011	0.016	0.277
Lactobacillus	Conc. of *B. animalis*	-0.039	-0.091	0.013	0.042
	Conc. of *L. reuteri*	***0.063**	0.011	0.115	0.038
	Conc. of Inulin	****0.013**	0.011	0.015	0.279
Streptococcus	Conc. of *B. animalis*	-0.060	-0.122	0.001	0.050
	Conc. of *L. reuteri*	-0.043	-0.104	0.018	0.052
	Conc. of Inulin	****-0.009**	-0.012	-0.007	0.162
Veillonella	Conc. of *B. animalis*	0.020	-0.018	0.058	0.005
	Conc. of *L. reuteri*	0.007	-0.031	0.045	0.005
	Conc. of Inulin	****-0.003**	-0.005	-0.002	0.041
Fusobacterium	Conc. of *B. animalis*	-0.004	-0.037	0.030	0.016
	Conc. of *L. reuteri*	0.011	-0.023	0.044	0.017
	Conc. of Inulin	****-0.006**	-0.007	-0.005	0.163
Parvimonas	Conc. of *B. animalis*	0.005	-0.008	0.019	0.002
	Conc. of *L. reuteri*	0.002	-0.011	0.016	0.002
	Conc. of Inulin	****-0.002**	-0.003	-0.002	0.122
Prevotella	Conc. of *B. animalis*	0.001	-0.007	0.008	0.026
	Conc. of *L. reuteri*	0.002	-0.006	0.009	0.027
	Conc. of Inulin	****-0.001**	-0.001	0.000	0.073

Table 2. Study population-level hierarchical multiple regression analysis. Overall effect of probiotic and prebiotic supplementation on relative abundance predictive values. *$p < 0.05$, **$p < 0.001$**.** Coef. values represent the predicted change in genus relative abundance per unit change in variable added to model. Concentrations (Conc.) of *B. animalis* and *L. reuteri* calculated as dilutions of initial broth culture with OD of 0.5. Concentration (Conc.) of inulin calculated as mg/ml.