Thank you for joining us!

WiFi Network Options: **IQGUEST** or **WFUBMCGUEST**

(no password required)

Fall Research Symposium:

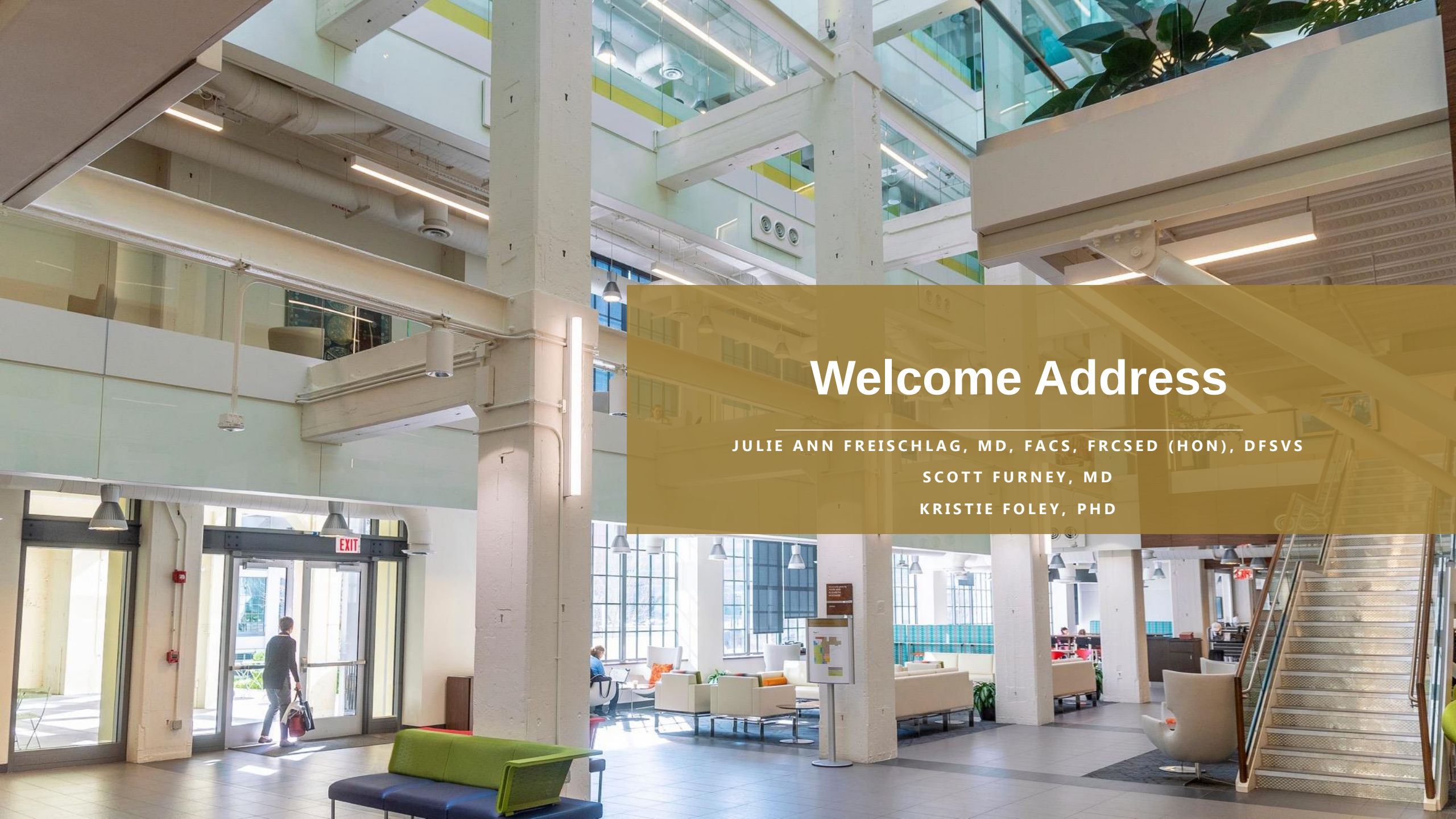
September 26, 2023 | 10:00am – 3:00pm

Jamy Ard, MD

Vice Dean for Clinical Research

Kristie Foley, PhD MS

Vice Dean for Research Strategy & Integration



Welcome Address

JULIE ANN FREISCHLAG, MD, FACS, FRCSED (HON), DFSVS

SCOTT FURNEY, MD

KRISTIE FOLEY, PHD

AGENDA

TIME	TOPIC	Presenters
10:00am	**Welcome Address**	Julie Ann Freischlag, MD, FACS, FRCSEd(Hon), DFSVS Scott Furney, MD Kristie Foley, PhD
10:10am	**Advocate National Center for Clinical Trials**	Jamy Ard, MD
10:15am	**Clinical Trial Presentations and Panel Discussion: Scalability & Health Equity**	Kristina Henderson Lewis, MD, MPH, SM Mia Yang, MD Kevin Gibbs, MD Cheryl Bushnell, MD
11:15am	**BREAK (Coffee Station:** Biotech Place Atrium**)**	
11:30am	**Clinical Trial Presentations and Panel Discussion: Scalability & Health Equity**	Michael T. Brennan, DDS Jonathan Schwartz, MD Joseph Skelton, MD, MS Stephen Park, MD
12:30pm	**Networking LUNCH:** Biotech Place Atrium	
1:15pm	**Clinical Trial Resource Offerings**	
	• **Data Infrastructure**	Emily Dressler, PhD
	• **Clinical Research Unit**	Jennifer Reeves, MHA, RN, BSN
	• **Integrating Special Populations**	Goldie Smith Byrd, PhD
	• **Working with Javara**	John Sanders, MS, MPH
1:45pm	**BREAK (Coffee Station:** Biotech Place Atrium**)**	
1:50pm	**Break Out Sessions**	Kevin High, MD & Kristie Foley, PhD | Jamy Ard, MD & Lynne Wagenknecht, DrPH
2:45pm	**Closing Remarks**	L. Ebony Boulware, MD, MPH

ADVOCATE HEALTH

Advocate National Center for Clinical Trials

POWERED BY

Wake Forest University School of Medicine

A Bold Vision

The Advocate National Center for Clinical Trials will deliver

- Enterprise excellence in full-scale, multi-site clinical trials
- State-of-the-art and next-generation capabilities
- Capabilities that are disease agnostic while building on significant enterprise strengths
- Streamlined administrative infrastructure and execution

ADVOCATE HEALTH

Transforming Clinical Trials

We can leverage our size and scale to be a one-stop solution for clinical trials

Full-scale, multi-site clinical trials

- Seamless execution of multi-site trials in **one health system**
- Multiple clinical settings with **wide geographic range**
- **Central** coordination and data management
- Covering **translational science spectrum**

ADVOCATE HEALTH

Transforming Clinical Trials

We will use our expertise to drive innovation in clinical trial conduct and lead healthcare discovery

State-of-the-art & next-gen capabilities

- Innovating in the science of clinical trial methodology
- Advanced study design, cohort selection, allocation, outcome assessment
- Best-in-class for **recruiting diverse populations**, analytics, and participant engagement

Disease agnostic, building on enterprise strengths

- Full **capabilities across a range of disease states** and disciplines
- Leverage strengths in cancer, CVD, aging, Alzheimer's, diabetes, obesity, and metabolism

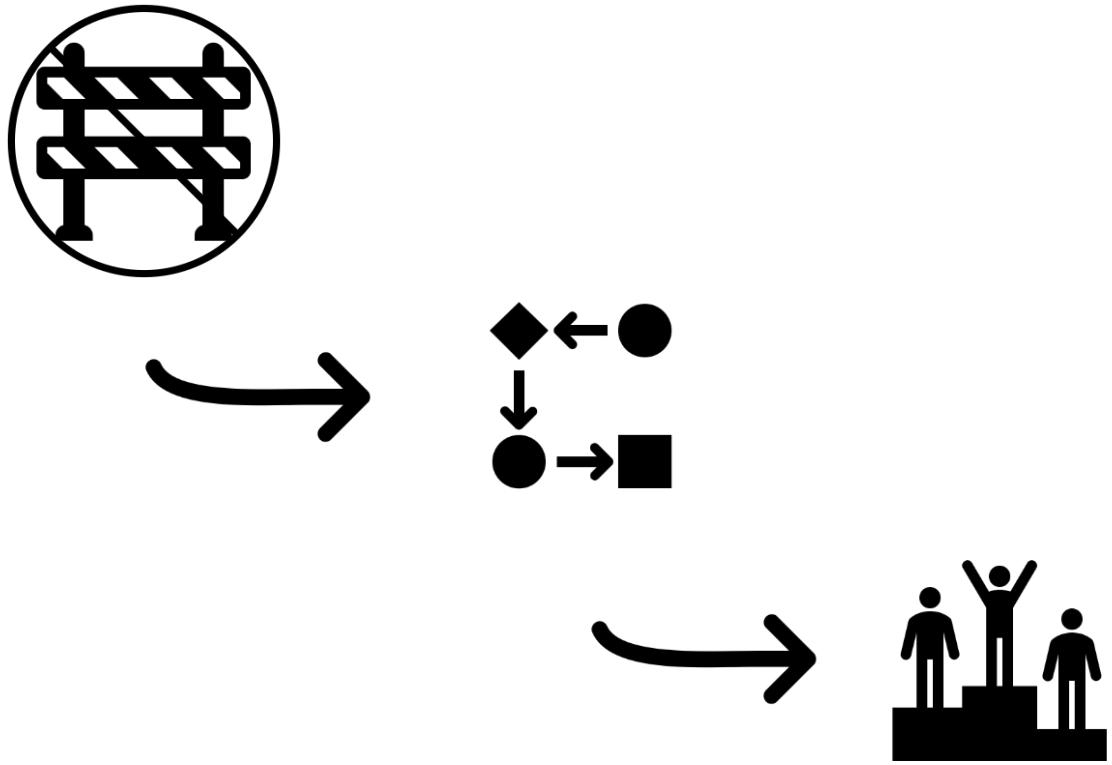
ADVOCATE HEALTH

Transforming Clinical Trials

We will have best-in-class operations that enable acceleration of our clinical trials program

Streamlined administrative infrastructure

- Eliminate hurdles for regulatory, grant, and contracting administration
- **Exceed sponsor expectations** for operational efficiency
- **Increase faculty productivity** and capacity
- Operate using a sustainable economic model



ADVOCATE HEALTH

Vision: Advocate National Center for Clinical Trials

powered by **Wake Forest University School of Medicine**

- We have many of the key components
- We will need strategic planning (process underway) and informed investment
- Investment will allow development/expansion of core capabilities
  (e.g., Enterprise Data Coordinating Center; Decentralized Trials Core; Shared Recruitment and Survey Service)
- Key differentiator for Advocate
  - Scale
  - Academic engine and integration
  - Impacting health and healthcare delivery

ADVOCATE HEALTH

Clinical Trial Presentations

KRISTINA HENDERSON LEWIS, MD, MPH, SM

MIA YANG, MD

KEVIN GIBBS, MD

CHERYL BUSHNELL, MD

A LEAP Forward for Obesity Treatment Access?

Kristina H. Lewis, MD MPH SM

Associate Professor

Division of Public Health Sciences

Obesity is a chronic relapsing disease

- Guidelines recommend **long-term treatment**

  - Lifestyle-based interventions → up to 50% non response ; up to **80% of initial responders regain** within 2 years

  - **Antiobesity Medication (AOM)** as adjunct if LBT not effective, for
    - BMI ≥ 30 kg/m^2 , or
    - BMI 27-29.9 kg/m^2 if a complication of excess weight is present (e.g. T2D)

CBS NEWS NEWS SHOWS LIVE LOCAL Login

MONEYWATCH ›

Even stronger obesity drug could further upend weight-loss care

MONEY WATCH

UPDATED ON: APRIL 27, 2023 / 9:15 PM / CBS/AP

THE WALL STREET JOURNAL. SIGN IN

t-Loss Drugs Is Coming

ul treatment on the market. To develop it, the drug company eld but failing practices

The cost? Up to $2,000 per month

npr wfdd

NEWS CULTURE MUSIC PODCASTS & SHOWS

BUSINESS

'You forget to eat': How Ozempic went from diabetes medicine to blockbuster diet drug

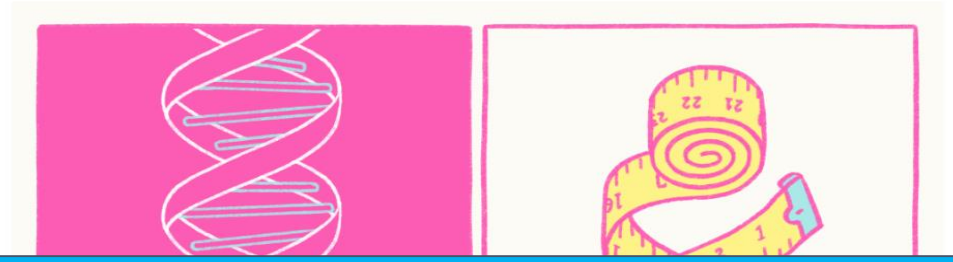
April 1, 2023 · 5:00 AM ET

The New York Times

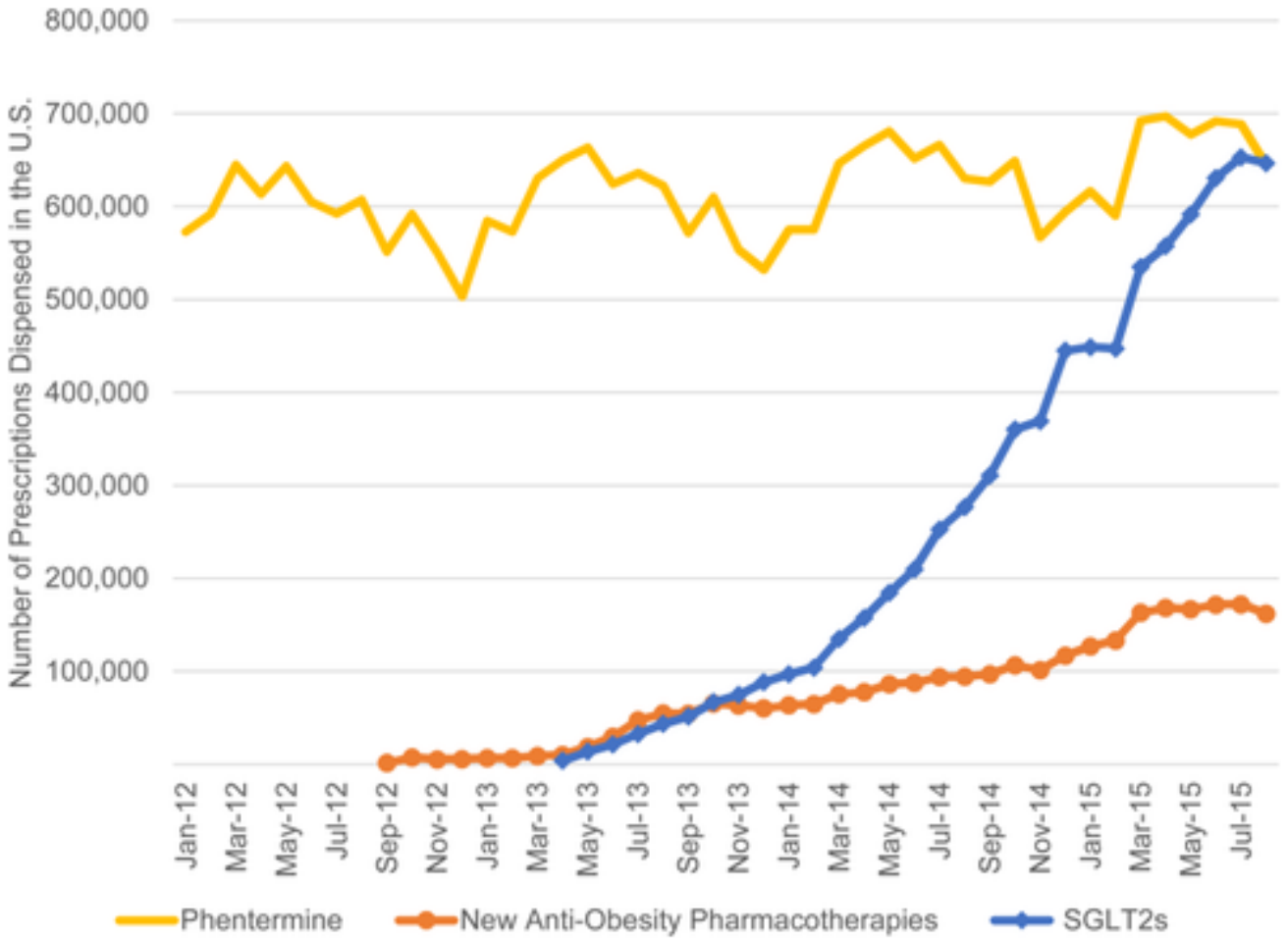
OPINION
GUEST ESSAY

w Weight Loss Drugs Teach bout Fat and Free Will

Jan. 31, 2023



Despite new medications, as of 2022, generic $5/month phentermine still accounts for the majority of fills in the U.S.

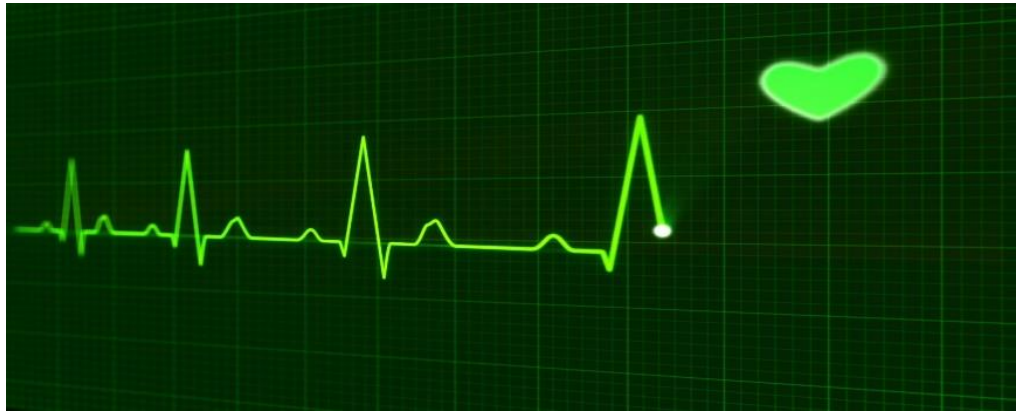


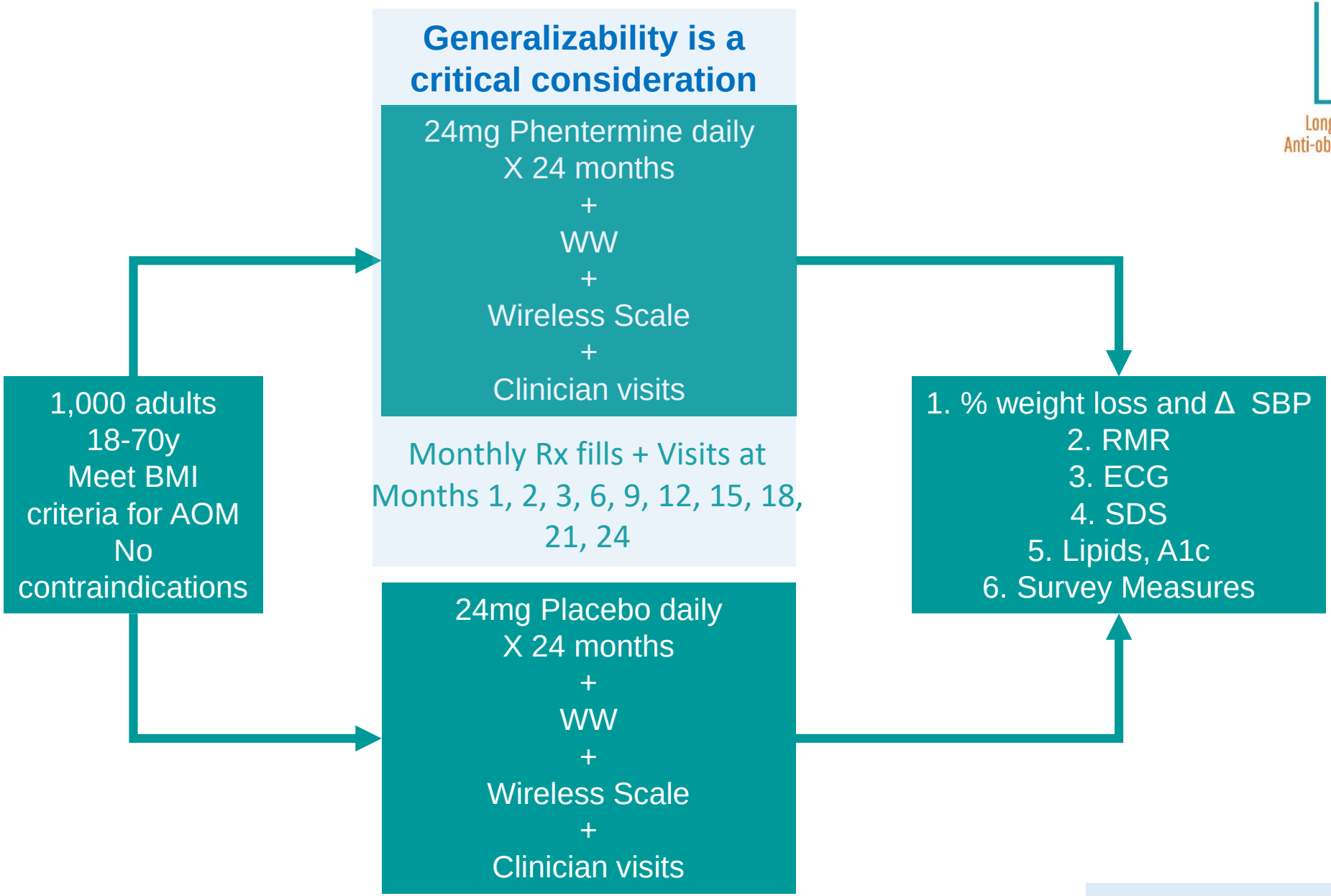
Obesity, Volume: 24, Issue: 9, Pages: 1955-1961, First published: 29 August 2016, DOI: (10.1002/oby.21533)

Thomas et al. *Obesity* 2016 September ; 24(9): 1955–1961. doi:10.1002/oby.21533

Question: Is longer term phentermine safe and effective?

- No randomized clinical trial data beyond 36 weeks
- Perceptions of high risk persist (blood pressure, heart disease and addiction concerns)
- Current policy limits broader, long-term use
  - 3-month duration on package insert





Long-term Effectiveness of the Anti-obesity medication Phentermine

4 Sites: AHWFB (WS + GSO), KP SoCal, Univ Texas, HealthPartners

CCC: Ard, Lewis
DCC: Pajewski

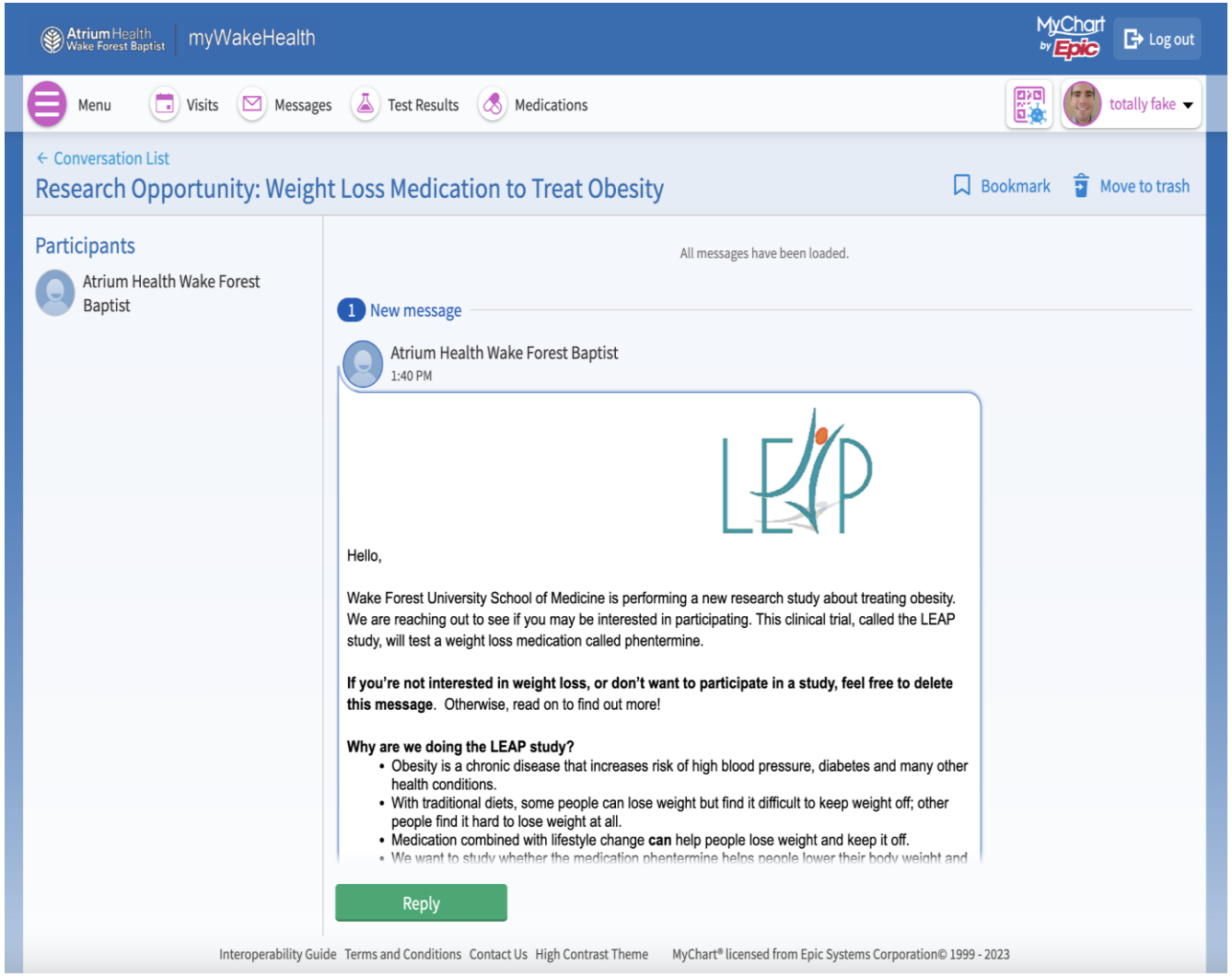
NIH Budget has not kept pace with inflation -
We are being asked to do more with substantially less staff time than historical trials – we must innovate for efficiency

Using the EHR to Identify Potential Participants

- Development of a **computable phenotype**
  - A “template” or “recipe” applied to a large dataset to select patients who meet criteria
    - Characteristics (e.g. age, sex, clinic site)
    - Specific clinical events or diagnoses (e.g. BMI, diabetes, heart failure)
  - Identify potentially-eligible patients with **greater speed and lower overall cost** than traditional manual chart reviews

Using MyWakeHealth for Recruitment

- Requires approval from **DCOMM**
- For LEAP:
  - Unique list pulled every 3 weeks with 1500 MRNs of potentially eligible participants
  - Each week, **~300 automated messages go out via MyWakeHealth to likely eligible patients**
  - Takes about 10 minutes of our staff's time per week…..



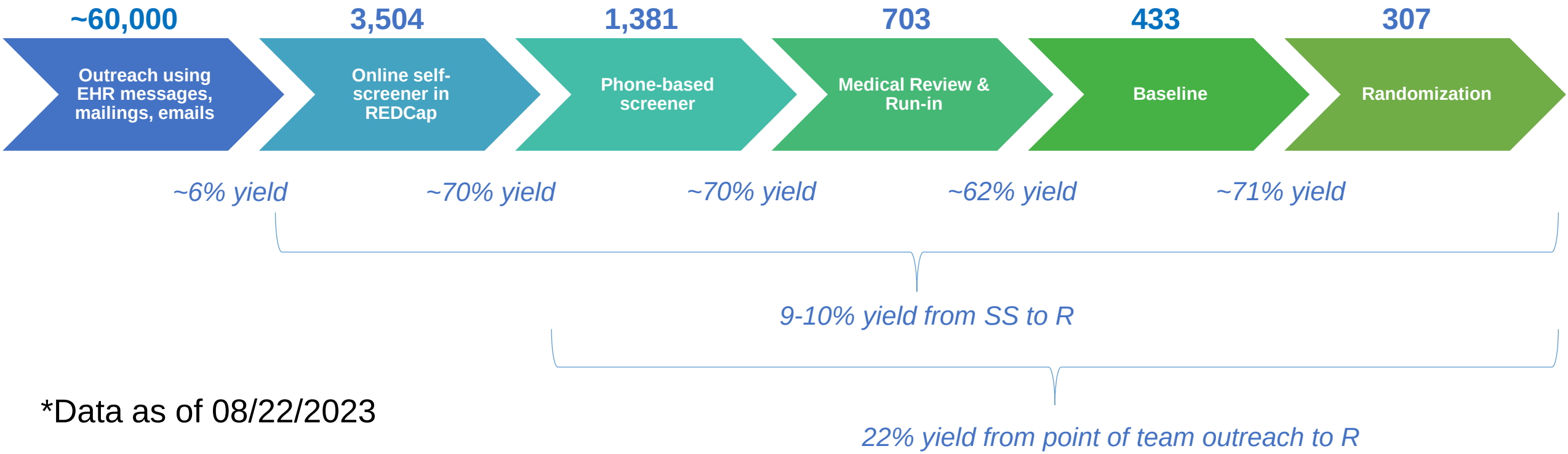
REDCap Self Screening Tool

- Patients can complete by:
  - Clicking link in myWakeHealth message, or
  - Scanning QR code in paper mailing
- Additional eligibility criteria not addressed by EHR phenotype
- Only once someone has successfully completed the self-screener in REDCap do our staff initiate outreach

Record ID	Screening						Behavioral Run-In Day 1	Behavioral Run-In Day 2	Behavioral Run-In Day 3	Behavioral Run-In Day 4	Behavioral Run-In Day 5
	LEAP ELIGIBILITY SELF-SCREENER SHORTENED	LEAP interest tracker	SV1- LEAP ELIGIBILITY INTERVIEWER ADMINISTERED	Run-in Contact Information	Medical Review Form	CURRENT STATUS OF PARTICIPANT	Behavioral Run-in	Behavioral Run-in	Behavioral Run-in	Behavioral Run-in	Behavioral Run-in
1252											
1253											
1254											
1255											
1256											
1257											
1258											
1259											
1260											
1261											
1262											
1263											
1264											
1265											
1266											
1267											

Record ID	1254
Are you currently interested in losing weight? * must provide value	Yes / No
Are you willing to take a medication by mouth (a pill) to help you lose weight? * must provide value	Yes / No
Monthly in-person visits for the LEAP study will take place at the following location: 4614 Country Club Road Winston-Salem, NC, 27104 **Would you be able to complete visits on a monthly basis at that location over the next 2 years (24 months)?** * must provide value	Yes / No
All of the study materials and communication with study staff will be in English. Are you comfortable with this? * must provide value	Yes / No
What is your current age in years? * must provide value	Less than 18 years old / 18-35 years old / 36-49 years old / 50-70 years old / 71 years or older
Please enter your current height in inches. **You can use this table to help convert feet and inches, to inches:**	

Flow of potentially-eligible participants



*Data as of 08/22/2023

Lessons Learned

Automating front end outreach for trials using:

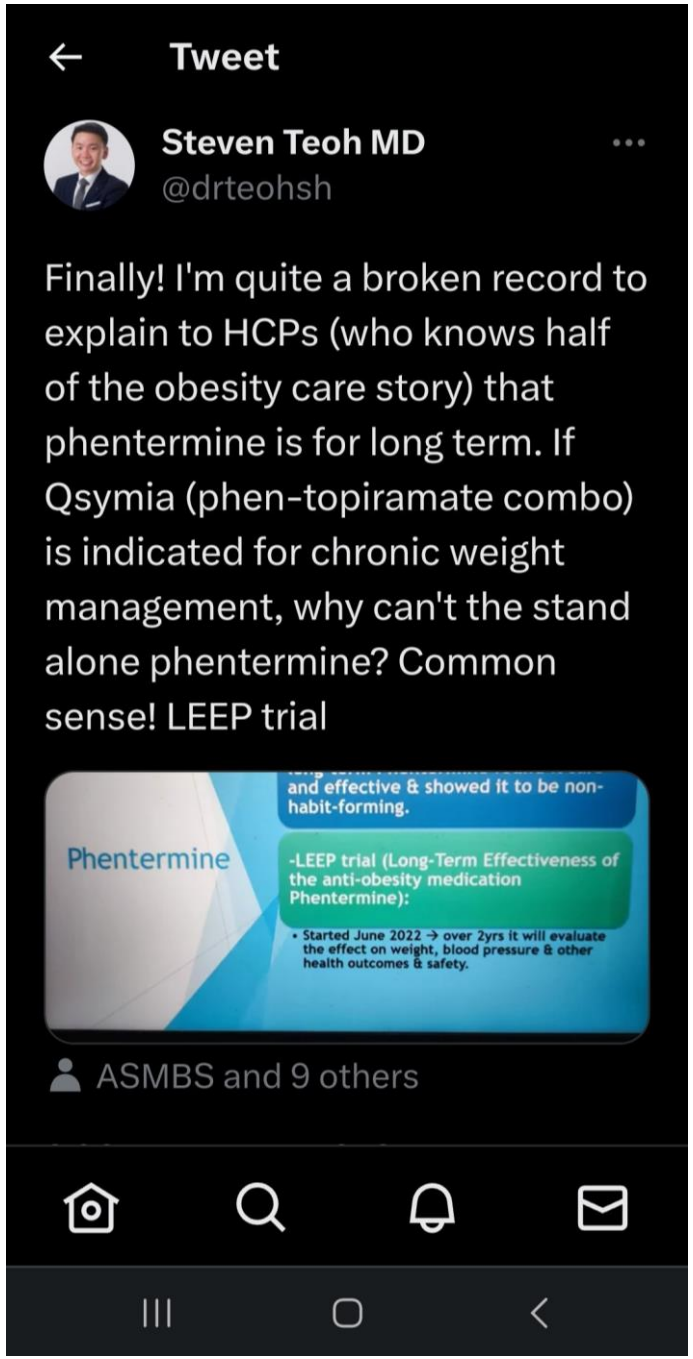
- EHR phenotyping
- myWakeHealth Messaging
- REDCap for self-screening

Streamlines staff effort and ↑s efficiency of recruitment

Future Needs to Support Additional Trials

- Standardized toolkits for trial startup
  - MOP chapter templates
  - Participant resources that have worked in other trials
  - Centralized training resources for staff on common trial measures
    - Blood pressure
    - ECG

- EHR use for capturing research measures
  - As opposed to building a completely separate study website
  - Could facilitate and have implications for data sharing under new NIH rules



LEEP
Long-term Effectiveness of the Anti-obesity medication Phentermine

- **New Trials in the Pipeline**
  - Plan to conduct future studies entirely within Atrium

Extra slides

Creating an EHR Phenotype

- **Goal** : Automate pre-screening of potentially eligible patients to **increase recruitment yield** and **decrease staff and participant screening burden**

- **Key points for consideration**:
  - Casts a wide net (prioritize sensitivity over specificity at this phase)
  - May under-represent patients who do not use the healthcare system regularly / not directly represent community sample

Translational Data Warehouse

- Integrates data from EHR and other sources; includes clinical data like demographics, diagnoses, procedures, medications, lab results, vitals, and visit details (historical and current).
- More complex data pulls can be performed by or with help from CTSI personnel (may be cost involved)

Number & Characteristics of Potentially Eligible Persons at Each Clinical Site				
	WFSM	UT	HP	KPSC
N eligible*	44,747	71,774	295,983	57,398
N/% by Age Group				
18-34y	5285 (12%)	16350 (23%)	63913 (22%)	12921 (23%
35-49y	10665 (24%)	20309 (28%)	87166 (29%)	15594 (27%)
50-64y	20845 (47%)	24636 (34%)	108279 (37%)	20504 (36%)
65-70y	7952 (18%)	10479 (15%)	36625 (12%)	8007 (15%)
N/% by BMI Category				
27-29.9	8529 (19%)	8816 (12%)	31377 (11%)	9628 (17%)
30-34.9	20184 (45%)	34564 (48%)	153564 (52%)	27780 (48%)
35-39.9	10897 (24%)	18148 (25%)	74325 (25%)	13868 (24%)
40-44.9	5137 (12%)	10246 (14%)	36717 (12%)	6122 (11%)
N/% Female	24124 (54%)	45361 (63%)	157191 (53%)	33798 (59%)
N/% Hispanic/LatinX	1936 (4%)	8747 (12%)	12601 (4%)	22836 (40%)
N/% Non-Hispanic Black	7625 (17%)	17705 (25%)	27768 (9%)	22938 (40%)
N/% Non-Hispanic White	33669 (75%)	29674 (41%)	189722 (64%)	7553 (13%)
*based on preliminary EHR data using age, BMI/comorbidity criteria for guideline based AOM prescribing				

Selected Baseline Characteristics of 307 Randomized Participants	
Characteristic	**% or Mean (SD)**
Age (years)	48.4 (12.6)
Male Sex	26.6%
Black or African American	18.6%
Hispanic	15.3%
Less than college education	42.4%
BMI (kg/m^2)	35.6 (4.0)
Pre-Diabetes or Type 2 Diabetes	29.2%
Essential Hypertension	33.7%

Dementia Care (D-CARE) Study: pragmatic clinical trial from operations to policy change

Mia Yang, MD MS

The Dementia Care Study
DCARE
Supporting Individuals and Caregivers

9/26/2023 | Gerontology & Geriatric Medicine

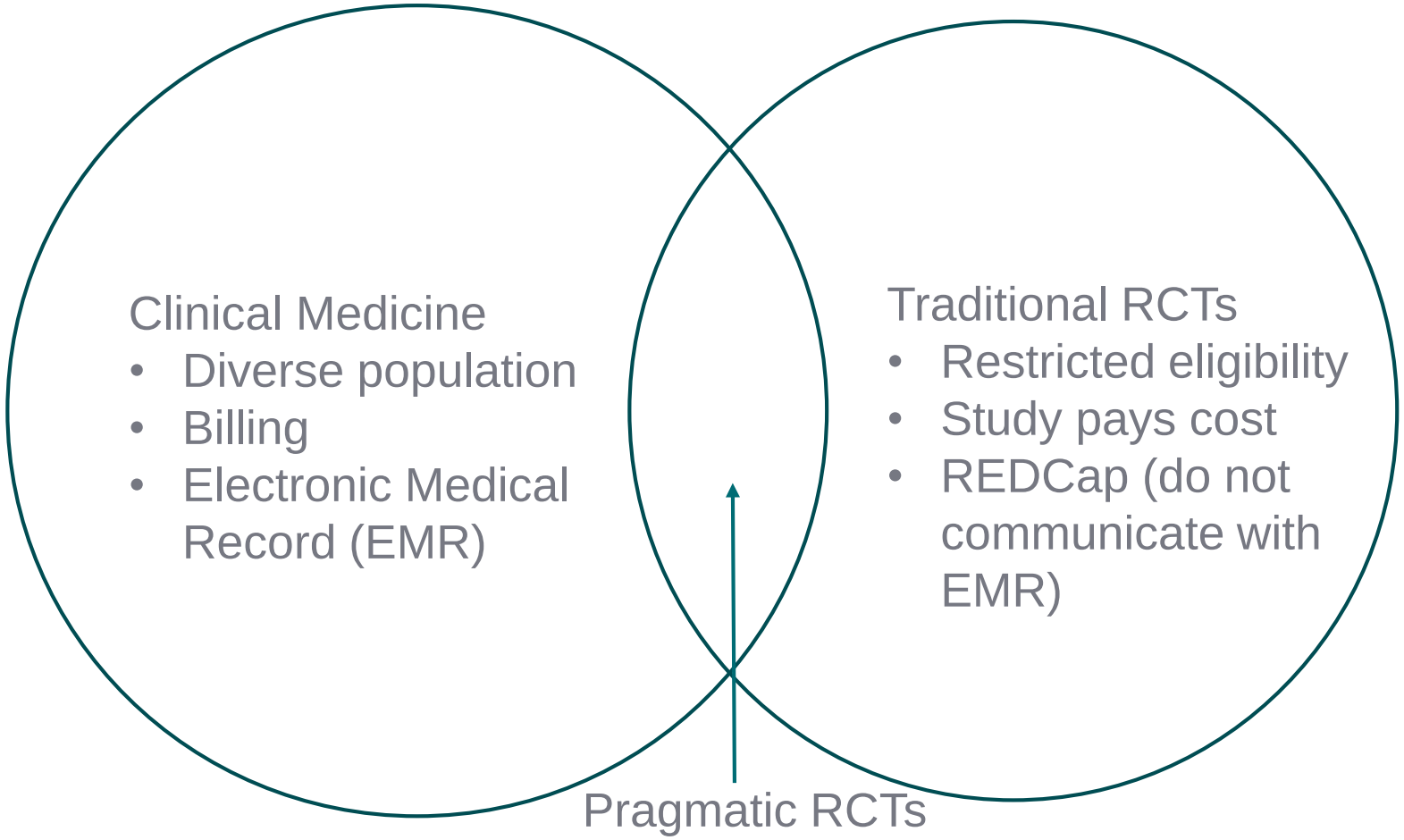
Current Dementia Care is Poor

- Dementia affects ALL other medical comorbidities' self management + financial, legal ramifications
- Dyadic relationships: medical & social needs rely on care partners to deliver

- <50% have had an evaluation for dementia
- <50% are told about the diagnosis of dementia
- Ineffective partnerships with community services

Callahan CM et al. Ann Intern Med 1995. Boustani M et al. JGIM 2005.
Boustani M. et al. J Gen Intern Med 2007. Alzheimer's Disease Facts 2021

D-CARE Study: Large, Diverse, & Pragmatic



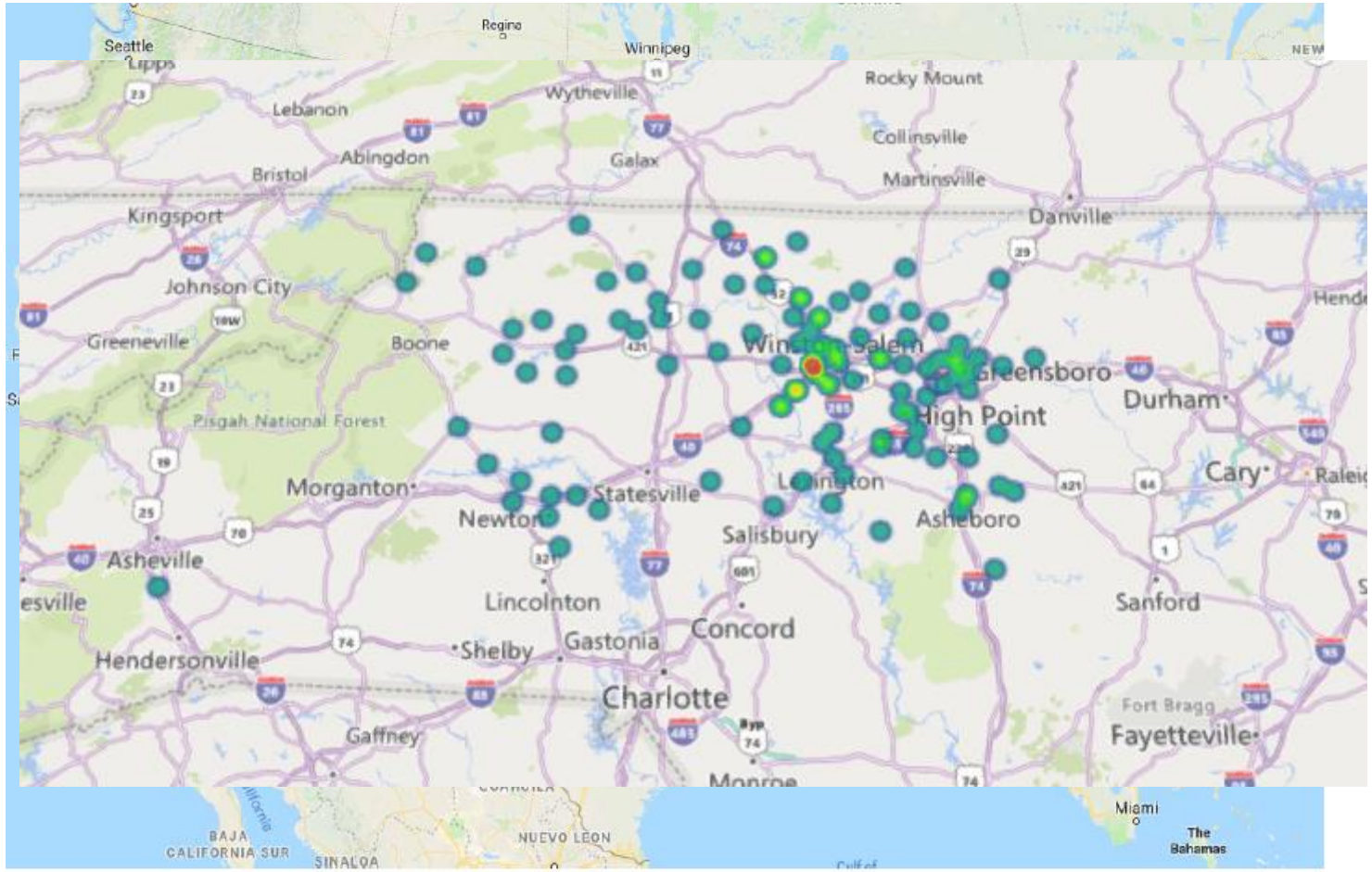
N: 2,150 dyads

Diverse: 21% Black + Latinos

Pragmatic: both research assessments & clinical/routine assessments

- Use EMR to recruit

Clinical Trial Sites & Coordinating Centers



Wake Forest® School of Medicine

Atrium Health Wake Forest Baptist

Intervention: Both Evidence-based Randomized to 7:7:1 Over 18 Months

Both have evidence of benefitting care partners

*Community-based Dementia Care	*Health-system Dementia Care	Usual Care
• Local non-profit • Social worker • Study covers cost	• 4 health systems • NPs, PAs • Bill for encounters • Rx	• Alzheimer's Association hotline • List of local resources*

*Based on Benjamin Rose Institute model

*Based on UCLA Alzheimer's & Dementia Care model

Final recruitment by site

(completed on January 31, 2022)

Clinical Trial Site	Total Participants Enrolled
Wake Forest University	837
Baylor Scott & White Health	626
University of Texas Medical Branch	478
Geisinger Health	235
Total	2,176

Baseline Outcomes

PLWD (N=2,176)	Overall Study	WF site
Age mean (SD)	80.6 (8.5)	80.4 (8.5)
Female	58.4%	56.9%
Hispanic	8.8%	1.1%
Black/African American	11.9%	13.3%
White	84.5%	84.5%
Black or Hispanic	20.6%	14.3%
High school or less	44.3%	43.5%
Lives alone	17.7%	19.4%

Care Partners (N = 2,176)	Overall Study	WF site
Age mean (SD)	65 (12.3)	65.1 (11.9)
Female	75.8%	75.6%
Black or Hispanic	20.8%	14.7%
High school or less	19.5%	17%
Spouse	44.7%	44%
Adult child	49%	49.3%
Lives with patient	73%	69.2%

ADC Alzheimer's and Dementia Care PROGRAM

The Dementia Care Study DCARE Supporting Individuals and Caregivers

A Stage IV and V Success Story

Type of Care	Impact
Hospitalizations	▼ 12%
ED visits	▼ 20%*
ICU stays	▼ 21%
Hospital days	▼ 26%*
Nursing home placement	▼ 40%*
Hospice in last 6 months	▲ 60%*

Total Medicare Costs of Care
▼ $2,404/year *

* p<.05, Based on NORC external evaluation of CMMI Award using fee-for-service claims data and UCLA ACO data September 2015 - September 2017

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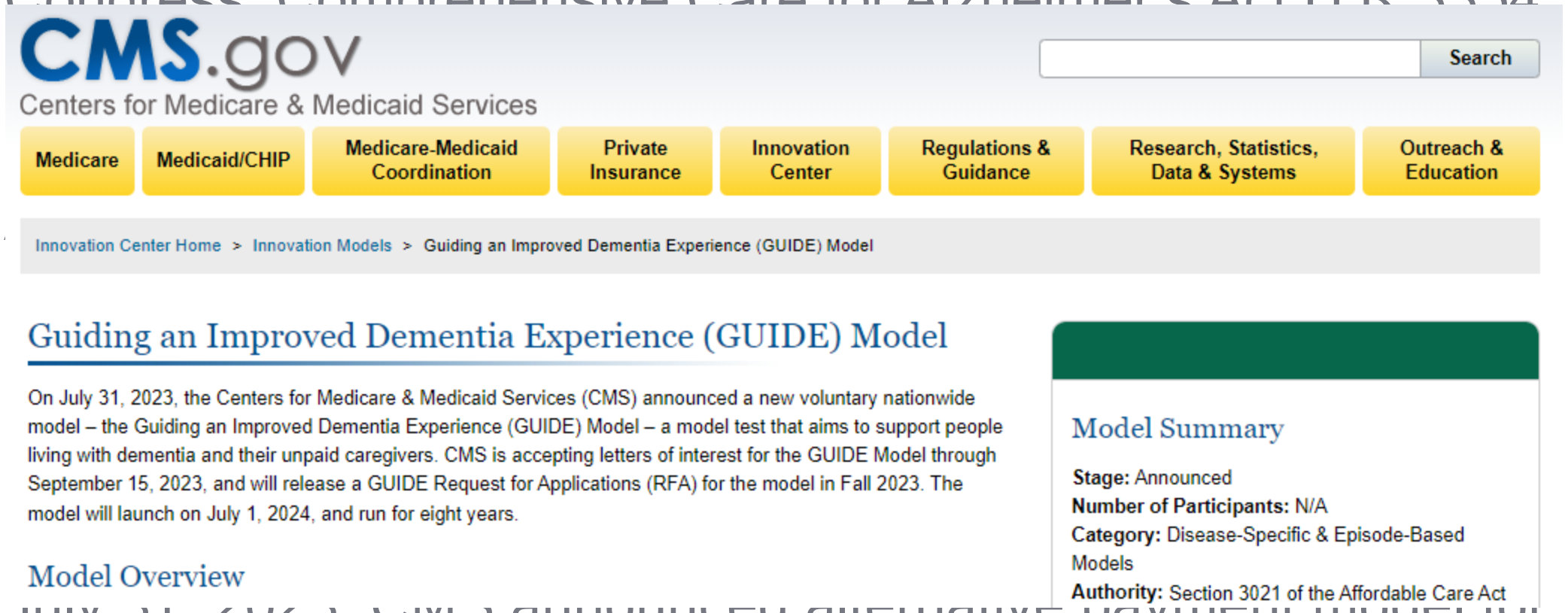
Atrium Health

Study advocacy for policy change:

- Congress: Comprehensive Care for Alzheimer's Act H.R. 3354
- July 31, 2023: CMS announced alternative payment model for comprehensive dementia care



Model Purpose and Overview

The GUIDE Model will test whether a comprehensive package of care coordination and management, caregiver support and education, and respite services can **improve quality of life for people with dementia and their caregivers** while **delaying avoidable long-term nursing home care** and **enabling more people to remain at home** through end of life.

Care Coordination & Management

Beneficiaries will receive care from an **interdisciplinary team** that will develop and implement a comprehensive, person-centered care plan for **managing the beneficiary's dementia and co-occurring conditions** and provide **ongoing monitoring and support.**

Caregiver Support & Education

GUIDE participants will provide a **caregiver support program**, which must include caregiver skills training, dementia diagnosis education, support groups, and access to a personal care navigator who can help problem solve and connect the caregiver to services and supports.

Respite Services

A subset of beneficiaries in the model will be eligible to receive payment for respite services with no cost sharing, up to a cap of **$2,500 per year**. These services may be provided to beneficiaries in a variety of settings, including **their personal home, an adult day center, and facilities that can provide 24-hour care** to give the caregiver a break from caring for the beneficiary.

Care Delivery Requirements

Participants must provide specified services across the domains outlined below. Participants will tailor the exact mix of services based on each beneficiary's individual care plan.

COMPREHENSIVE ASSESSMENT
Beneficiaries and caregivers receive separate assessments to identify their needs and a home visit to assess the beneficiary's safety.

CARE PLAN
Beneficiaries receive care plans that address their goals, preferences, and needs, which helps them feel certain about next steps.

24/7 ACCESS
Beneficiaries and caregivers can call a member of their care team or a third-party representative using a 24/7 helpline.

ONGOING MONITORING & SUPPORT
Care navigators provide long-term help to beneficiaries and caregivers so they can revisit their goals and needs at any time and are not left alone in the process.

REFERRAL & SUPPORT COORDINATION
Beneficiaries' care navigator connects them and their caregivers to community-based services and supports, such as home-delivered meals and transportation.

CAREGIVER SUPPORT
Caregivers take educational classes and beneficiaries receive respite services, which helps relieve the burden of caregiving duties.

MEDICATION MANAGEMENT
Clinician reviews and reconciles medication as needed; care navigators provide tips for beneficiaries to maintain the correct medication schedule.

CARE COORDINATION & TRANSITION
Beneficiaries receive timely referrals to specialists to address other health issues, such as diabetes, and the care navigators coordinate care with the specialist.

CMS
CENTER FOR MEDICARE & MEDICAID INNOVATION

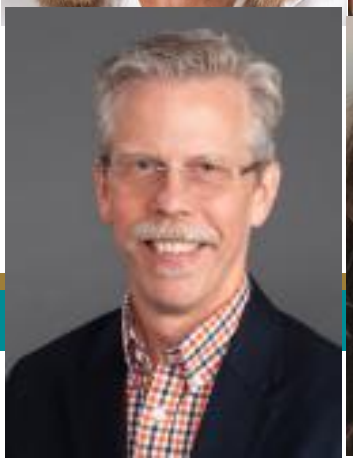
Wake Forest® School of Medicine

Atrium Health

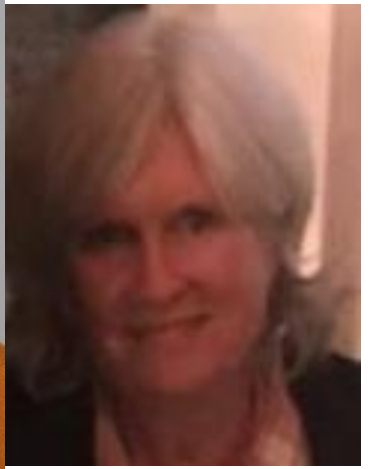
Thanks to WF D-CARE team!

miyang@wakehealth.edu








Patient-centered Outcomes research Institute

pcori

The Dementia Care Study
DCARE
Supporting Individuals and Caregivers

NIH National Institute on Aging

Comparative Effectiveness Pragmatic Trials in the Acutely Ill

KEVIN GIBBS MD

ASSOCIATE PROFESSOR

DIRECTOR OF MEDICAL ICU CLINICAL TRIALS

SECTION ON PULMONARY CRITICAL CARE ALLERGY IMMUNOLOGY

DISCLOSURES

- Salary Support from the NIH and DOD
- Pragmatic Critical Care Research Group (PCCRG) executive committee member

What are Pragmatic Comparative Effectiveness Trials?

- Clinicians often face clinical problems with multiple standard of care therapies and insufficient evidence to guide decision making
- Comparative effectiveness trials test relative efficacy of 2 or more standard of care therapies
- Pragmatism
  - Imbedded in routine clinical care
  - Screening, enrollment, and in some cases data collection, are performed by clinical staff
  - ‘Light touch’ by research personnel

The DEVICE trial

Video vs Direct Laryngoscopy in Emergency Tracheal Intubation

- Planned enrollment of 2000 critically ill patients
- 17 EDs and ICUs across the country
  - WF Baptist ED and MICU
- Primary outcome: 1st pass success

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Video versus Direct Laryngoscopy for Tracheal Intubation of Critically Ill Adults

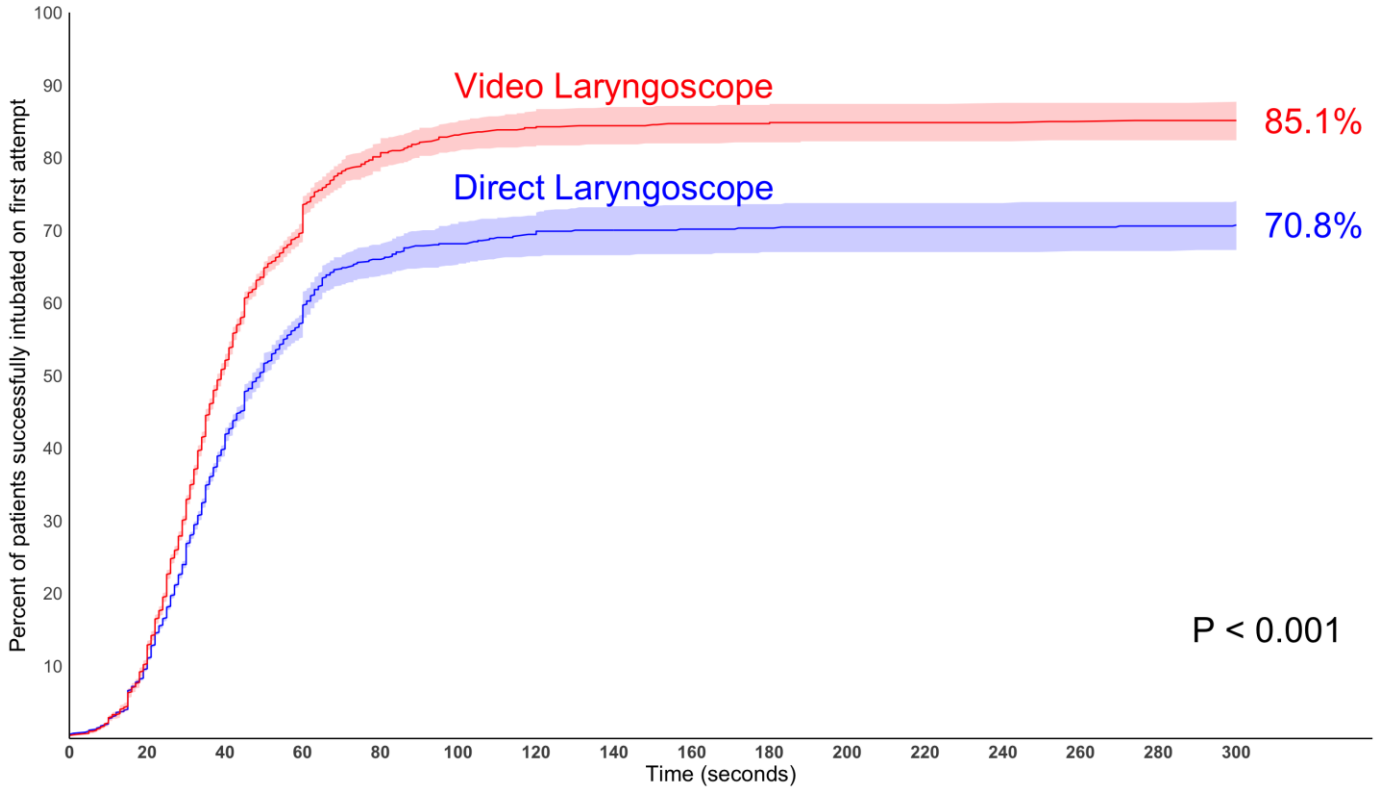
M.E. Prekker, B.E. Driver, S.A. Trent, D. Resnick-Ault, K.P. Seitz, D.W. Russell, J.P. Gaillard, A.J. Latimer, S.A. Ghamande, K.W. Gibbs, D.J. Vonderhaar, M.R. Whitson, C.R. Barnes, J.P. Walco, I.S. Douglas, V. Krishnamoorthy, A. Dagan, J.J. Bastman, B.D. Lloyd, S. Gandotra, J.K. Goranson, S.H. Mitchell, H.D. White, J.A. Palakshappa, A. Espinera, D.B. Page, A. Joffe, S.J. Hansen, C.G. Hughes, T. George, J.T. Herbert, N.I. Shapiro, S.G. Schauer, B.J. Long, B. Imhoff, L. Wang, J.P. Rhoads, K.N. Womack, D.R. Janz, W.H. Self, T.W. Rice, A.A. Ginde, J.D. Casey, and M.W. Semler, for the DEVICE Investigators and the Pragmatic Critical Care Research Group*

ABSTRACT

Pragmatic Critical Care Research Group

DEVICE
DirEct versus VIdeo laryngosCopE trial

- Enrolled 1400 patients in 8 months
- Stopped early for efficacy



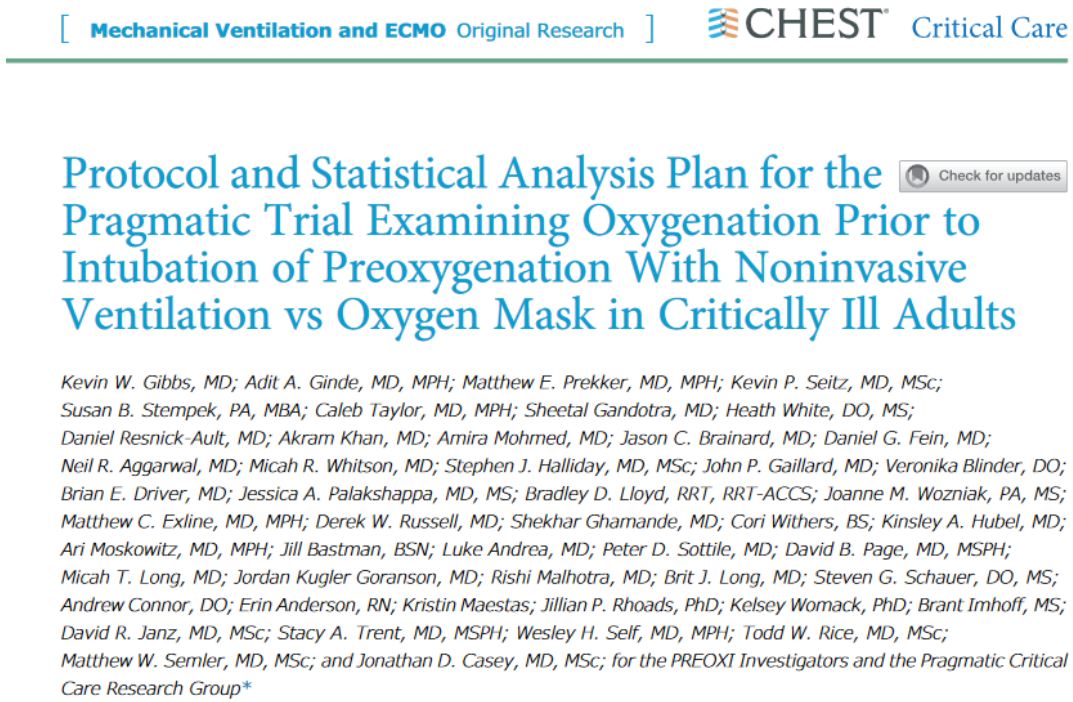
Atrium Health

Wake Forest University School of Medicine

The PREOXI Trial

Noninvasive ventilation vs oxygen mask preoxygenation

- Planned enrollment: 1300 subjects
- 24 EDs and ICUs across the country
  - WF ED and MICU
  - Gibbs Protocol chair
- Primary outcome: Incidence of Hypoxemia



[Mechanical Ventilation and ECMO Original Research] CHEST Critical Care

Protocol and Statistical Analysis Plan for the Pragmatic Trial Examining Oxygenation Prior to Intubation of Preoxygenation With Noninvasive Ventilation vs Oxygen Mask in Critically Ill Adults

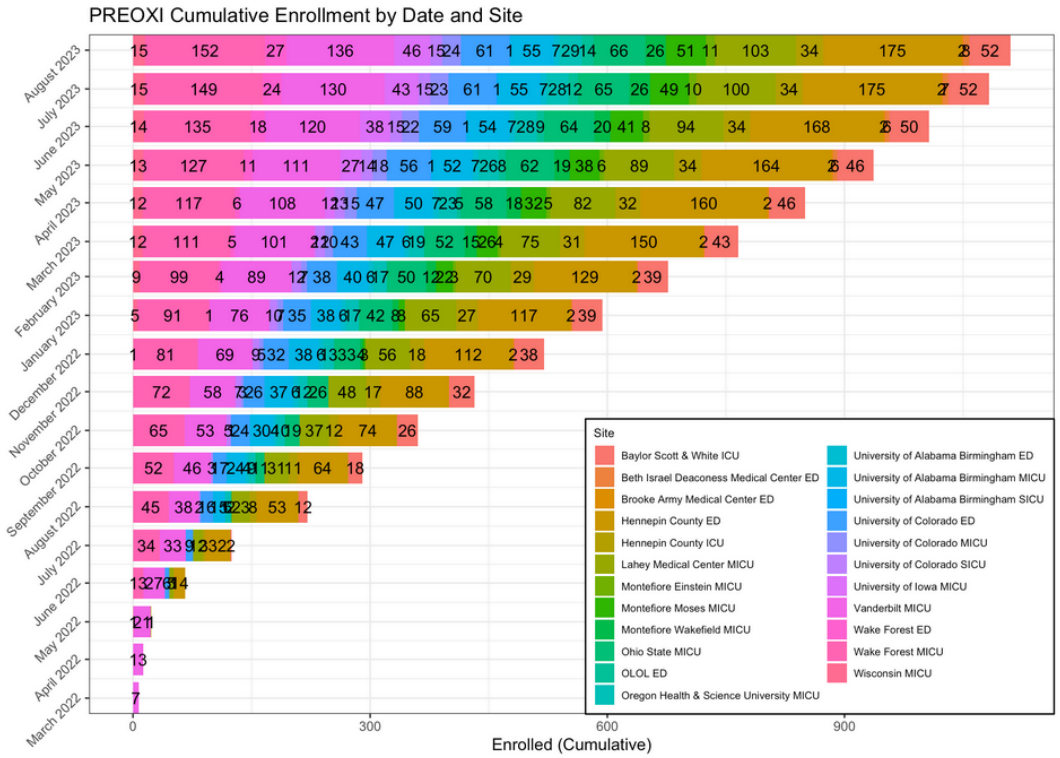
Check for updates

*Kevin W. Gibbs, MD; Adit A. Ginde, MD, MPH; Matthew E. Prekker, MD, MPH; Kevin P. Seitz, MD, MSc; Susan B. Stempek, PA, MBA; Caleb Taylor, MD, MPH; Sheetal Gandotra, MD; Heath White, DO, MS; Daniel Resnick-Ault, MD; Akram Khan, MD; Amira Mohmed, MD; Jason C. Brainard, MD; Daniel G. Fein, MD; Neil R. Aggarwal, MD; Micah R. Whitson, MD; Stephen J. Halliday, MD, MSc; John P. Gaillard, MD; Veronika Blinder, DO; Brian E. Driver, MD; Jessica A. Palakshappa, MD, MS; Bradley D. Lloyd, RRT, RRT-ACCS; Joanne M. Wozniak, PA, MS; Matthew C. Exline, MD, MPH; Derek W. Russell, MD; Shekhar Ghamande, MD; Cori Withers, BS; Kinsley A. Hubel, MD; Ari Moskowitz, MD, MPH; Jill Bastman, BSN; Luke Andrea, MD; Peter D. Sottile, MD; David B. Page, MD, MSPH; Micah T. Long, MD; Jordan Kugler Goranson, MD; Rishi Malhotra, MD; Brit J. Long, MD; Steven G. Schauer, DO, MS; Andrew Connor, DO; Erin Anderson, RN; Kristin Maestas; Jillian P. Rhoads, PhD; Kelsey Womack, PhD; Brant Imhoff, MS; David R. Janz, MD, MSc; Stacy A. Trent, MD, MSPH; Wesley H. Self, MD, MPH; Todd W. Rice, MD, MSc; Matthew W. Semler, MD, MSc; and Jonathan D. Casey, MD, MSc; for the PREOXI Investigators and the Pragmatic Critical Care Research Group**

Pragmatic Critical Care Research Group

PREOXI

- >1200 of 1300 patient enrolled to date (done in October)
- WF is the 2nd leading enroller



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The PIVOT-1 Trial

Adaptive Pressure Control vs Volume Control Mechanical Ventilation

- Single center sequential cluster cross-over trial
- Funded by the Wake Forest Critical Illness, Injury, and Recovery Research Center (CIIRRC)
  - $6000
- Statistical support by PHS (Dr. O'Connell)
- Primary outcome: Feasibility of unit-based cluster allocation


RESPIRATORY CARE

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A Pragmatic Pilot Trial Comparing Patient Triggered Adaptive Pressure Control to Patient Triggered Volume Control Ventilation in Critically ill Adults

Kevin W. Gibbs, Jonathan L. Forbes, Kelsey Harrison, Jennifer T.W. Krall, Aubrae Isenhart, Stephanie P. Taylor, R. Shayn Martin, Nathaniel S. O'Connell, Rita N. Bakhru, Jessica A. Palakshappa and D. Clark Files

Respiratory Care March 2023, respcare.10803; DOI: https://doi.org/10.4187/respcare.10803

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PIVOT-1

- Enrolled 137 subjects over 9 weeks
- Met feasibility outcome

Table 2: Primary and Exploratory Outcomes

	APC	AVC	P values
1st hour mode adherence (%[95% CI])	98[91-100]	94[86-98]	.14
24 hour mode adherence (%[95% CI])	95[91-100]	84[78-89]	**<.001**

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Upcoming Trials

Share

Research Awarded; Contract pending

Pragmatic Trial Comparing the Effectiveness of Ketamine versus Etomidate for Intubation

Sign Up for Updates

Protocol and statistical analysis plan for the Mode of Ventilation During Critical IllnEss (MODE) trial

Kevin P. Seitz, Bradley D. Lloyd, Li Wang, Matthew S. Shotwell, Edward T. Qian, Roger K. Richardson, Jeffery C. Rooks, Vanessa Hennings-Williams, Claire E. Sandoval, Whitney D. Richardson, Tracy Morgan, Amber N. Thompson, Pamela G. Hastings, Terry P. Ring, Joanna L. Stollings, Erica M. Talbot, David J. Krasinski, Bailey Decoursey, Kevin W. Gibbs, Wesley H. Self, Amanda S. Mixon, Todd W. Rice, Matthew W. Semler, Jonathan D. Casey

doi: https://doi.org/10.1101/2023.07.21.23292998

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

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Conclusion

- Comparative effectiveness research is important
- Pragmatically imbedding comparative effectiveness trials in routine clinical care in the acutely ill is feasible
- Our enterprise size uniquely positions us to definitively answer questions using pragmatic comparative methodology
  - I have a LOT of thoughts on this and am happy to discuss further

From Pragmatic Trial to Comparative Effectiveness: Maximizing Technology for Secondary Prevention of Stroke

Cheryl Bushnell, MD, MHS, Professor of Neurology, Vice-Chair for Research

Department of Neurology

Disclosures

- Dr. Bushnell has ownership in Care Directions, LLC
- Research funding from PCORI, NIH/NINDS, NIH/NICHD (relevant to topic) and NCATS (UL-1)

Objectives

- Describe the COMprehensive Post-Acute Stroke Services (COMPASS) pragmatic trial and the technology used
- The aLHS and technology approach in the transition from COMPASS to comparative effectiveness
- Describe the TEAMS-BP (Telehealth-Enhanced Assessment and Management after Stroke—Blood Pressure) feasibility trial, the expanded role of technology

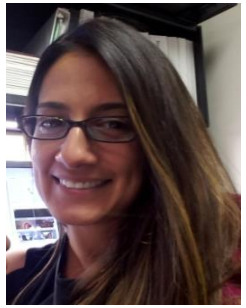
Pamela Duncan, PhD, PT, PI

Wayne Rosamond, PhD, co-PI

Cheryl Bushnell, MD, MHS, co-PI

COMprehensive Post-Acute Stroke Services (COMPASS)

Transitional care model tested in real world practice



Atrium Health Wake Forest Baptist

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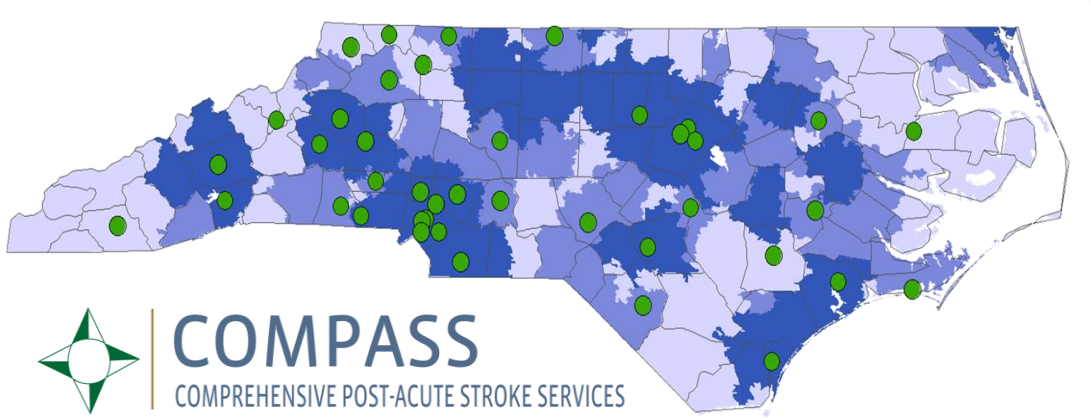
Pragmatic Trial of Transitional Care Management

- Cluster-randomized pragmatic trial
- 40 randomized hospital units in NC, stratified by stroke volume and Joint Commission Certification status
- 5,882 patients discharged home
- Transitional care implemented in clinical workflow, consistent with CMS policies and reimbursement



- **Primary outcome**: 90-day functional status using Stroke Impact Scale (SIS-16)

Duncan et al. *Circ Qual Cardiovasc Outcomes* 2020;13(6):e006285.

Intervention: A Comprehensive Care Model

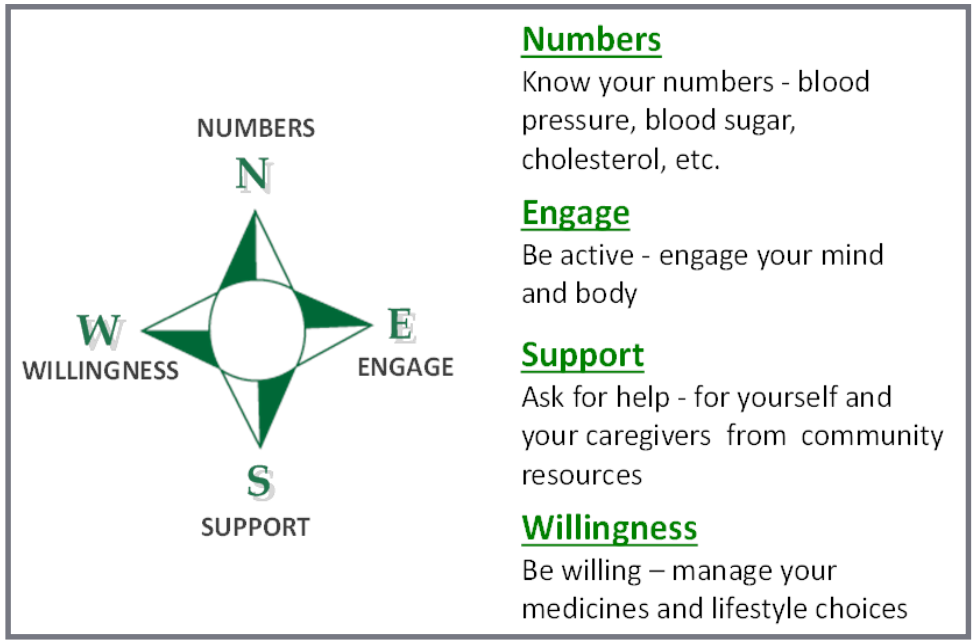
2 Day Call | Clinic Visit by Day 14 | 30 Day Call | 60 Day Call

Care Team:

- Advanced Practice Provider (APP) or Physician
- Post-Acute Care Nurse Coordinator (PAC)

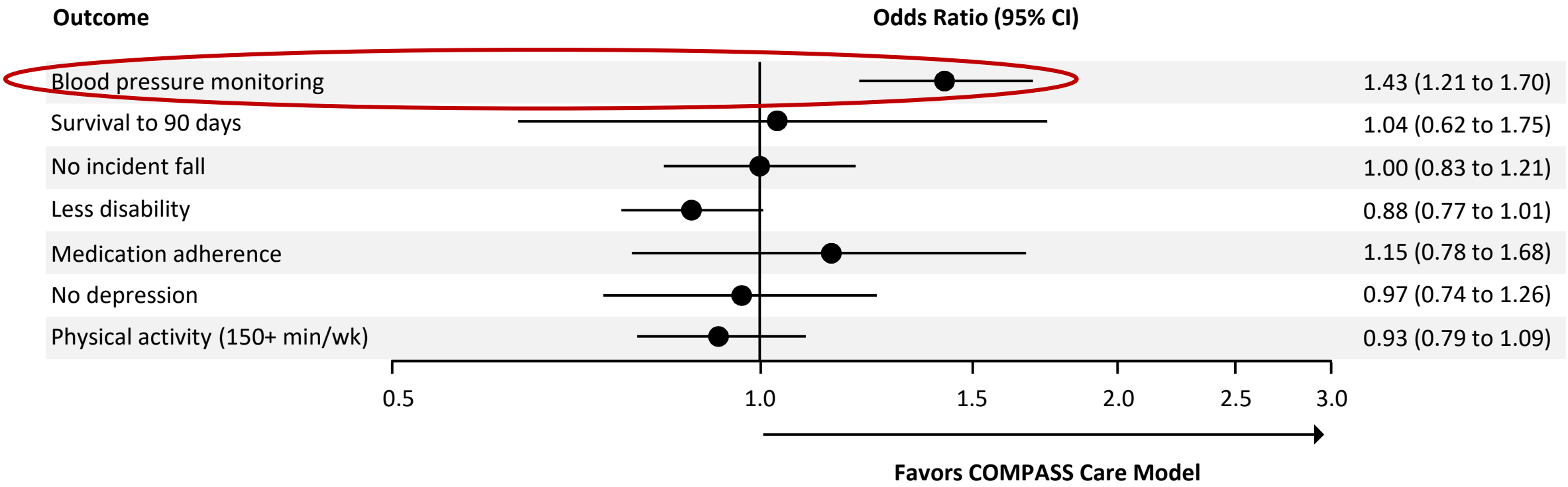
Intervention Highlights:

- Digital tool to assess functional and social determinants of self-management and health
- Individualized care plans:
  - Secondary Prevention
  - Rehabilitation and Recovery
  - Caregiver Support
  - Referrals to Community Resources
- Quality performance measures



Bushnell et al. *J Am Geriatr Soc*, 2018;66(5).

Results: ITT Secondary Outcomes: Categorical



However, only 35% of those randomized to hospitals in the intervention group received the intervention

Duncan et al. *Circ Qual Cardiovasc Outcomes* 2020;13(6): e006285.

Gesell *et al. BMC Health Services Research* (2019) 19:978
https://doi.org/10.1186/s12913-019-4771-0

BMC Health Services Research

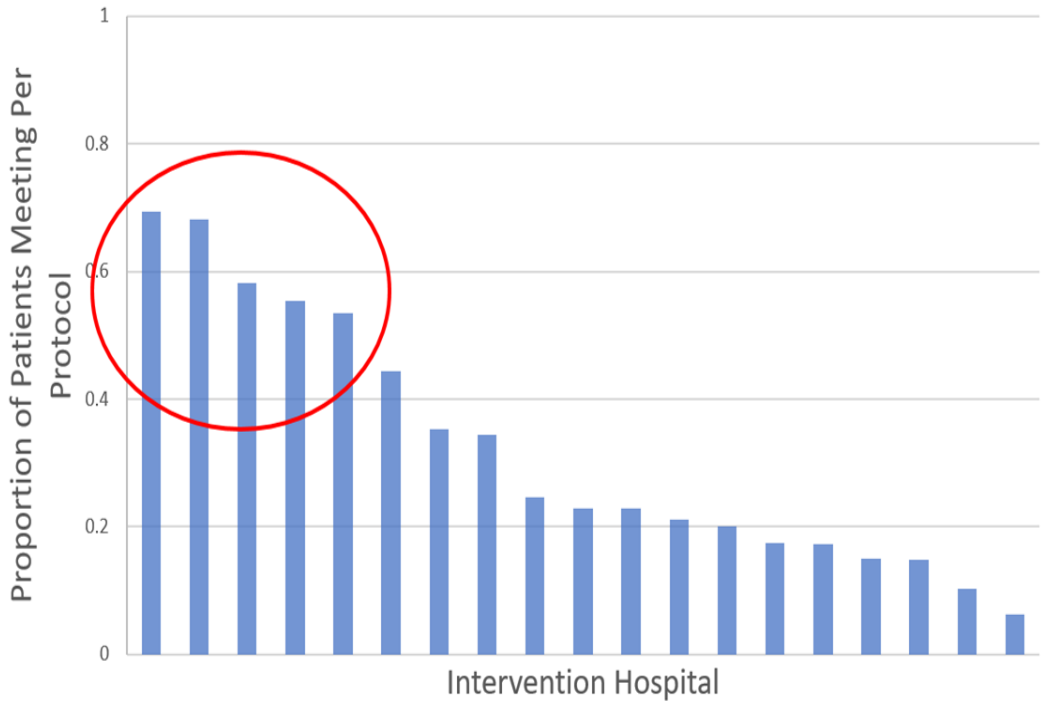
RESEARCH ARTICLE Open Access

Implementation of a billable transitional care model for stroke patients: the COMPASS study

Sabina B. Gesell[1*], Cheryl D. Bushnell[2], Sara B. Jones[3], Sylvia W. Coleman[2], Samantha M. Levy[4], James G. Xenakis[5], Barbara J. Lutz[6], Janet Prvu Bettger[7], Janet Freburger[8], Jacqueline R. Halladay[5], Anna M. Johnson[3], Anna M. Kucharska-Newton[3,9], Laurie H. Mettam[3], Amy M. Pastva[7], Matthew A. Psioda[4], Meghan D. Radman[2], Wayne D. Rosamond[3], Mysha E. Sissine[2], Joanne Halls[10] and Pamela W. Duncan[2]

- **System-level barriers**: consistent staffing, competing priorities, did not enroll or schedule patients prior to acute care hospital discharge.
- Only 58% of hospitals delivered the intervention uninterrupted.

Characteristics of Successful Sites: Implementation Analysis



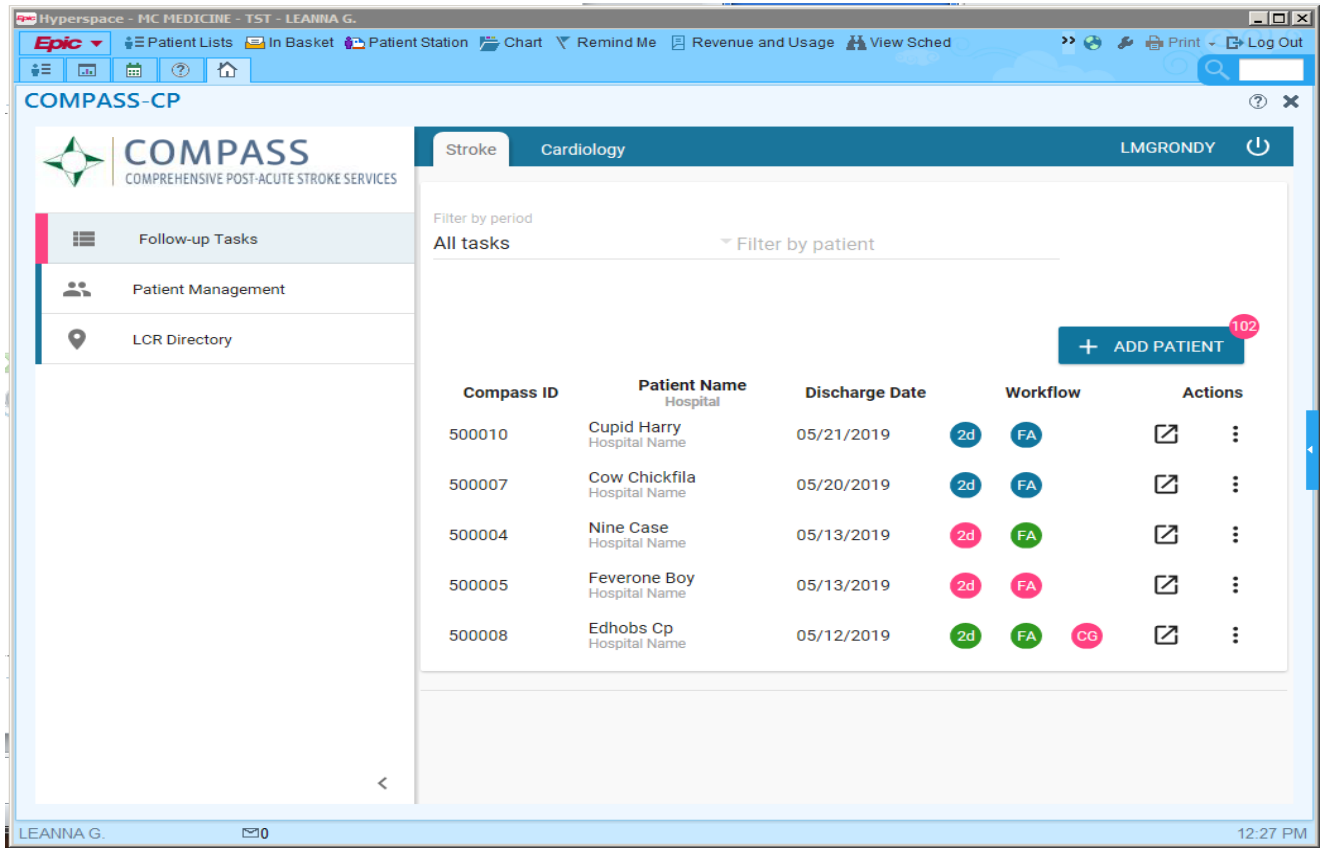
- **Commitment/Champion for the Model in Acute Care**
- Vision
- System Resources
- Flexibility/Collaboration
- Location of Practice (**Neurology Clinics**)
- New Standard of Care

Lutz et al. *Gerontologist,* 2020;60(6):1071-1084.

Care Plan Technology: Workable but not integrated with EHR

- Proprietary algorithms to assist with referrals to resources and shared decision-making were developed by PHS using SAS code
- Required logging into a separate system housed at UNC-CH
- Providers at recruiting sites also documented similar information in their EHRs for transitional care management billing

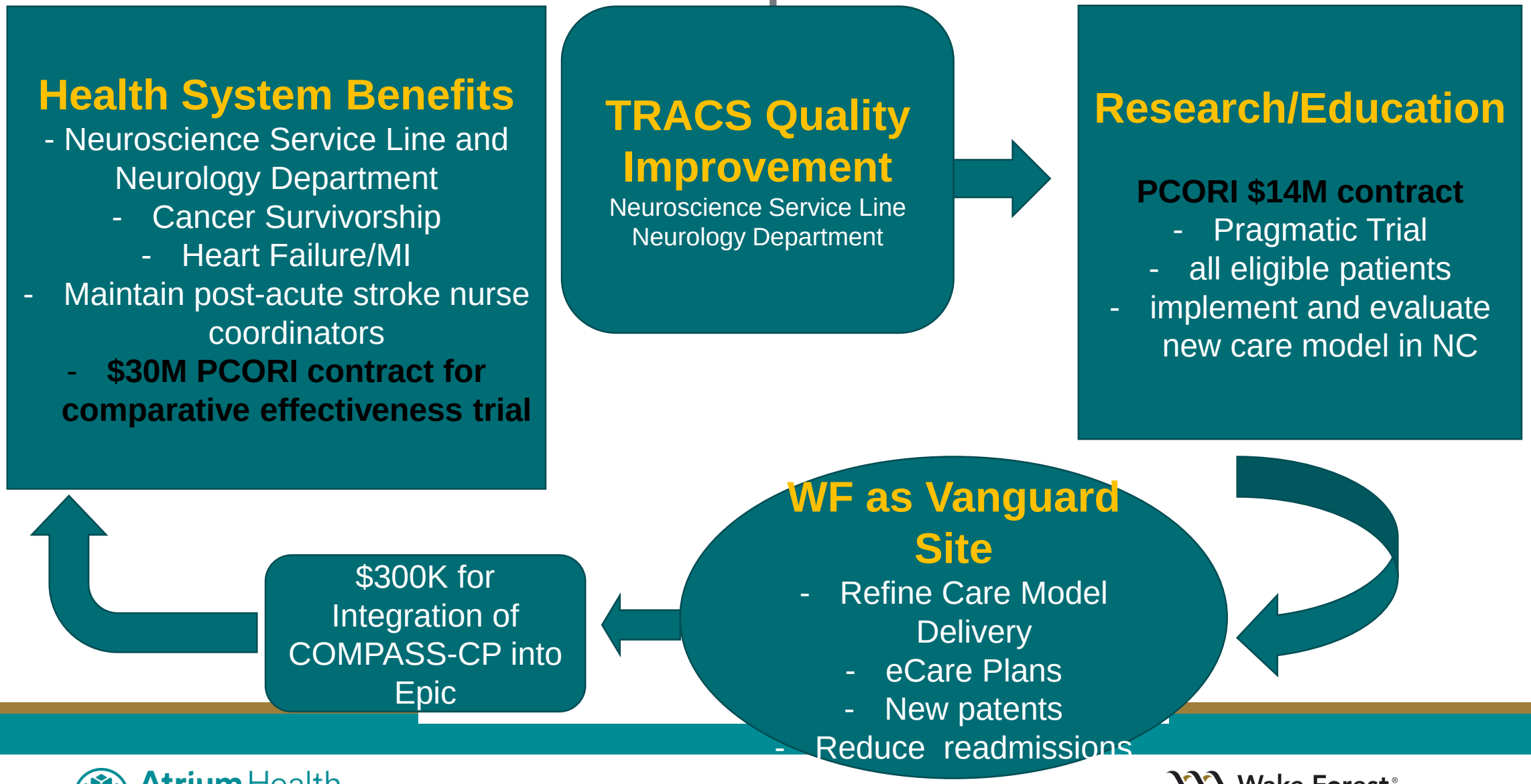
Advancements since the pragmatic trial



COMPASS-CP has been integrated into Epic and the clinical workflow

- Identifies patients with stroke ICD-10 codes in the hospital or ED

AHWFB aLHS Example



From COMPASS to Hypertension Management:

Telehealth-Enhanced Assessment and Management after Stroke—Blood Pressure (TEAMS-BP)

PCORI Phased Large Awards for Comparative Effectiveness Research (PLACER)

- Feasibility phase: 18 months and $2 million
  - Refine interventions with pilot study
  - Reassess sample size
  - Stakeholder input
  - Milestones
  - Interim progress reports q 6 months and final report for Expert Advisory Panel review and approval for full trial
- Full trial phase: 5 years and $20 million

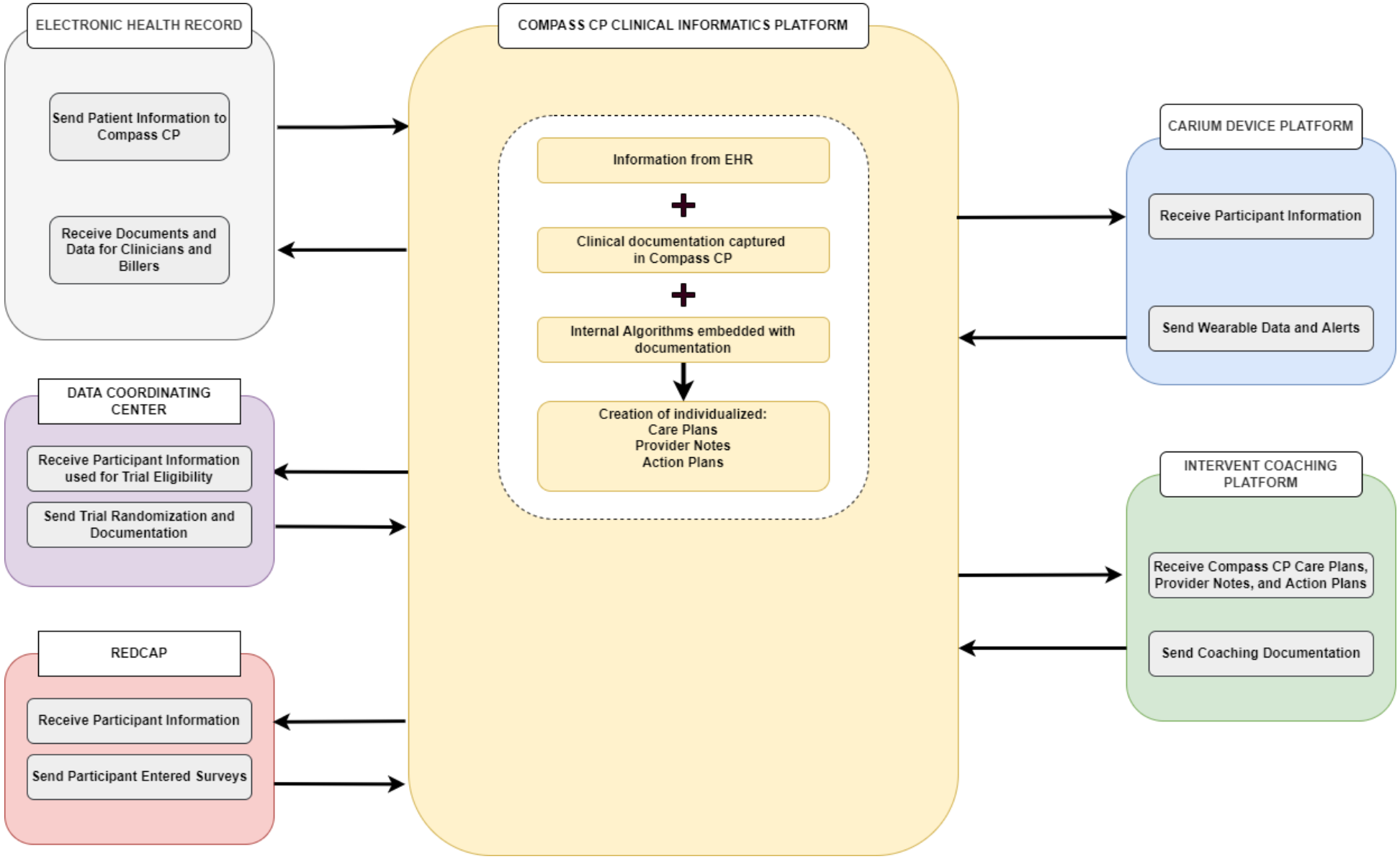
INTERVENTION COMPONENTS

	 TEAM-BASED MEDICAL MANAGEMENT	 BLOOD PRESSURE MONITORING	 HEALTHY LIFESTYLE COACHING	 PATIENT-CENTERED CARE PLANNING	 MEDICATION MANAGEMENT
INTENSIVE TAILORED TELEHEALTH MANAGEMENT	**Telehealth visits** & enrollment in **CCM / RPM**	**Remote transmission** of home BP measurements	**High-intensity** telephone-based lifestyle coaching supported by activity monitor	Comprehensive **BP Action Plan** – shared with providers and Health Coach	Reminders and support through **Carium notifications**
INTENSIVE CLINIC MANAGEMENT	**Clinic follow-up**	Participant maintained **paper log** of home BP measurements	**Low-intensity** lifestyle coaching supported by educational text messaging	**Standard COMPASS** care plan – shared with providers	Participant maintained **paper log** of medication taking behavior

Overall Specific Aims:

1. Compare effectiveness of ITTM v. ICM on reaching target of SBP ≤130 mm Hg 6-months post-stroke.
2. Compare effectiveness of ITTM v. ICM on improving major adverse cardiovascular events (MACE) and patient activation for BP management.
3. Determine whether ITTM or ICM is most effective at improving SBP and patient activation among:
   - African Americans
   - Patients with physical (mRankin ≥ 2) or cognitive (Montreal Cognitive Assessment ≤ 22) disability
   - Patients aged ≥75 years

TEAMS-BP Technology: COMPASS-CP as the Central Informatics Platform



Institutional and CTSI contributions to COMPASS and TEAMS-BP

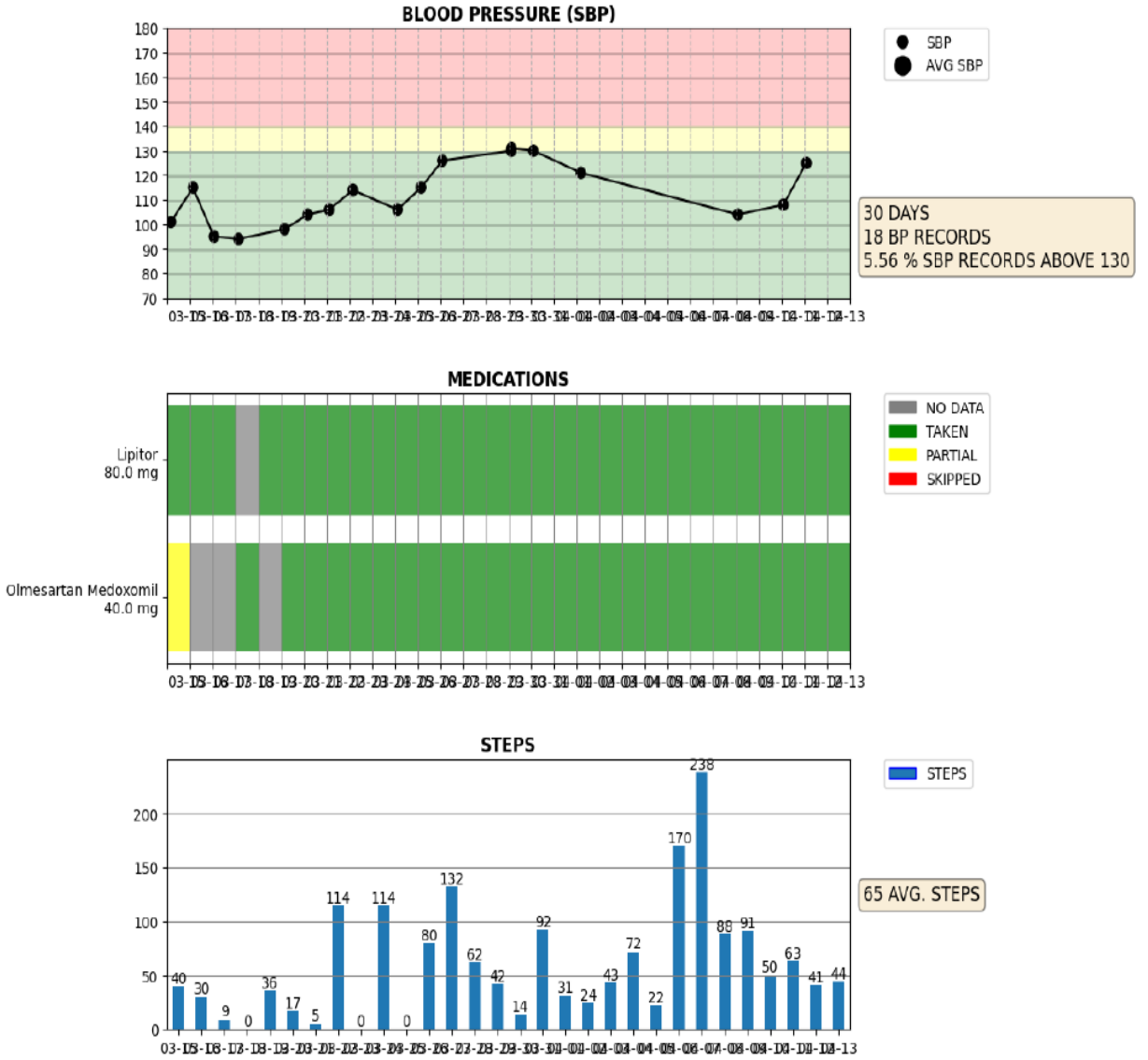
- Wake Forest Innovations funding for Epic-integration of COMPASS-CP
- Wake Forest IT team approving the integration
  - Umit Topaloglu, Mark Pemberton
- Supplemental institutional funds provide the necessary IT support for TEAMS-BP
  - Julie Freischlag, Chris O'Byrne, Terry Hales
- IRB support for the complex consent process in COMPASS and development of pre-consent for TEAMS-BP
  - Brian Moore

Key Feasibility Phase Accomplishments

- Met Feasibility Enrollment Goals: n=50 participants/3 sites
- Multiple process adaptations implemented to address barriers
- Successful delivery of both the ICM and ITTM arms of TEAMS-BP
- High participant satisfaction with the study in both arms
- Establishment of integrated or web-based approach for COMPASS utilization to facilitate data flow across study platforms
- Demonstrated ability to submit billing for Chronic Care Management supported by Lifestyle Coaching documentation

Key Feasibility Phase Technology Accomplishments

- Clinically relevant and usable Chronic Care Management and Remote Patient Monitoring Data sent at regular intervals to provider and participant through the Carium mobile phone app



Acknowledgements

- Pam Duncan, PhD, PT
- Christina Condon, MSN, NP-C
- Sabina Gesell, PhD
- COMPASS team
- Stakeholders: Gladys Lundy-Lamm and Typhany Morrison-Brooks
- Scott Rushing, Matthew Redhair, TEAMS-BP IT team

Panel Discussion

SCALABILITY

AND

HEALTH EQUITY

BREAK

BIOTECH PLACE ATRIUM

Clinical Trial Presentations

MICHAEL T. BRENNAN, DDS

JONATHAN SCHWARTZ, MD

JOSEPH SKELTON, MD, MS

STEPHEN PARK, MD

Gene Therapy for the Treatment of Radiation-Induced Xerostomia

MIKE BRENNAN DDS, MHS

Chair, Dept. of Oral Medicine/Oral & Maxillofacial Surgery

Atrium Health Carolinas Medical Center

Charlotte, NC USA

Professor, Dept or Otolaryngology/Head & Neck Surgery

Wake Forest University School of Medicine

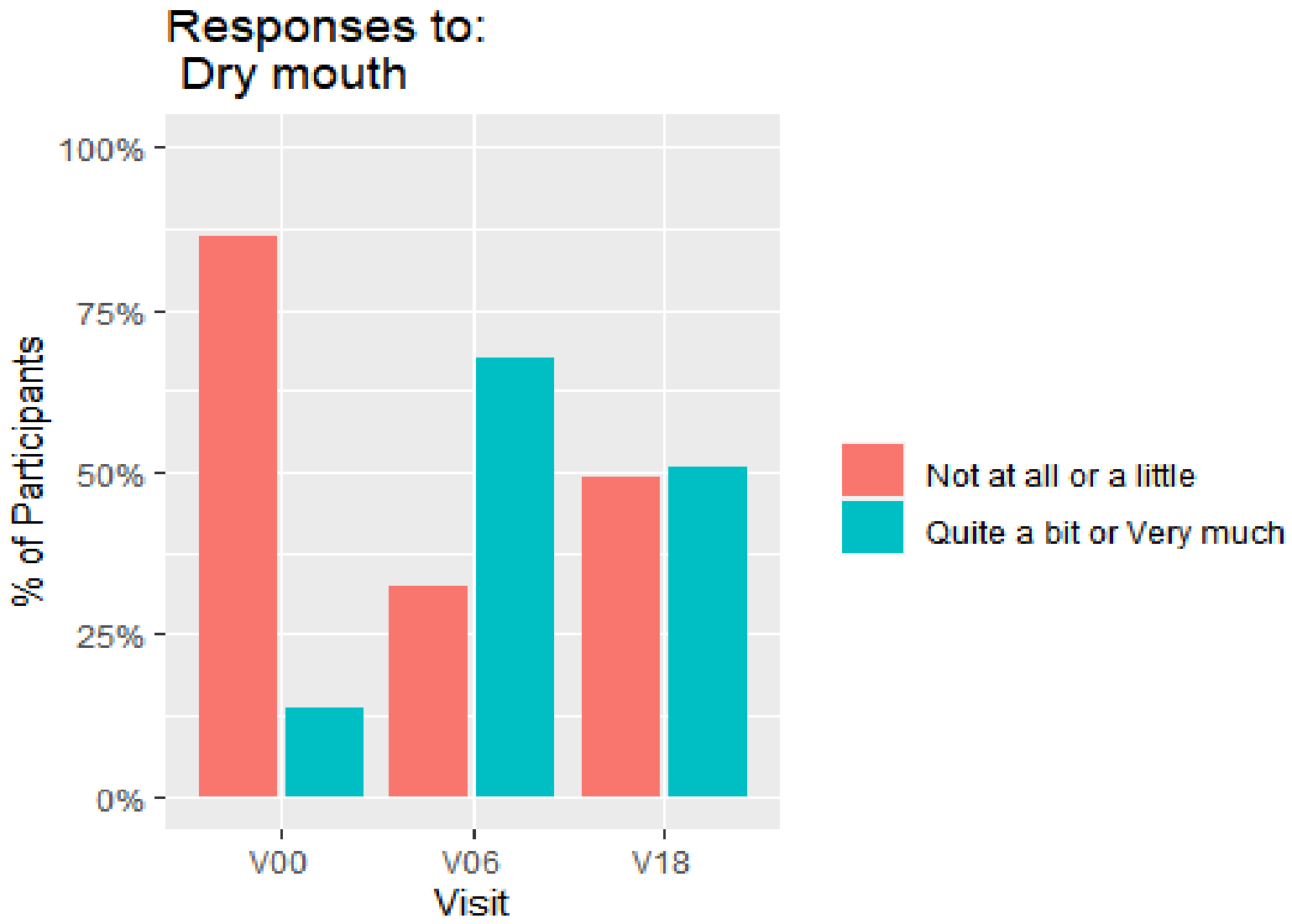
Winston-Salem, NC USA

Disclosures

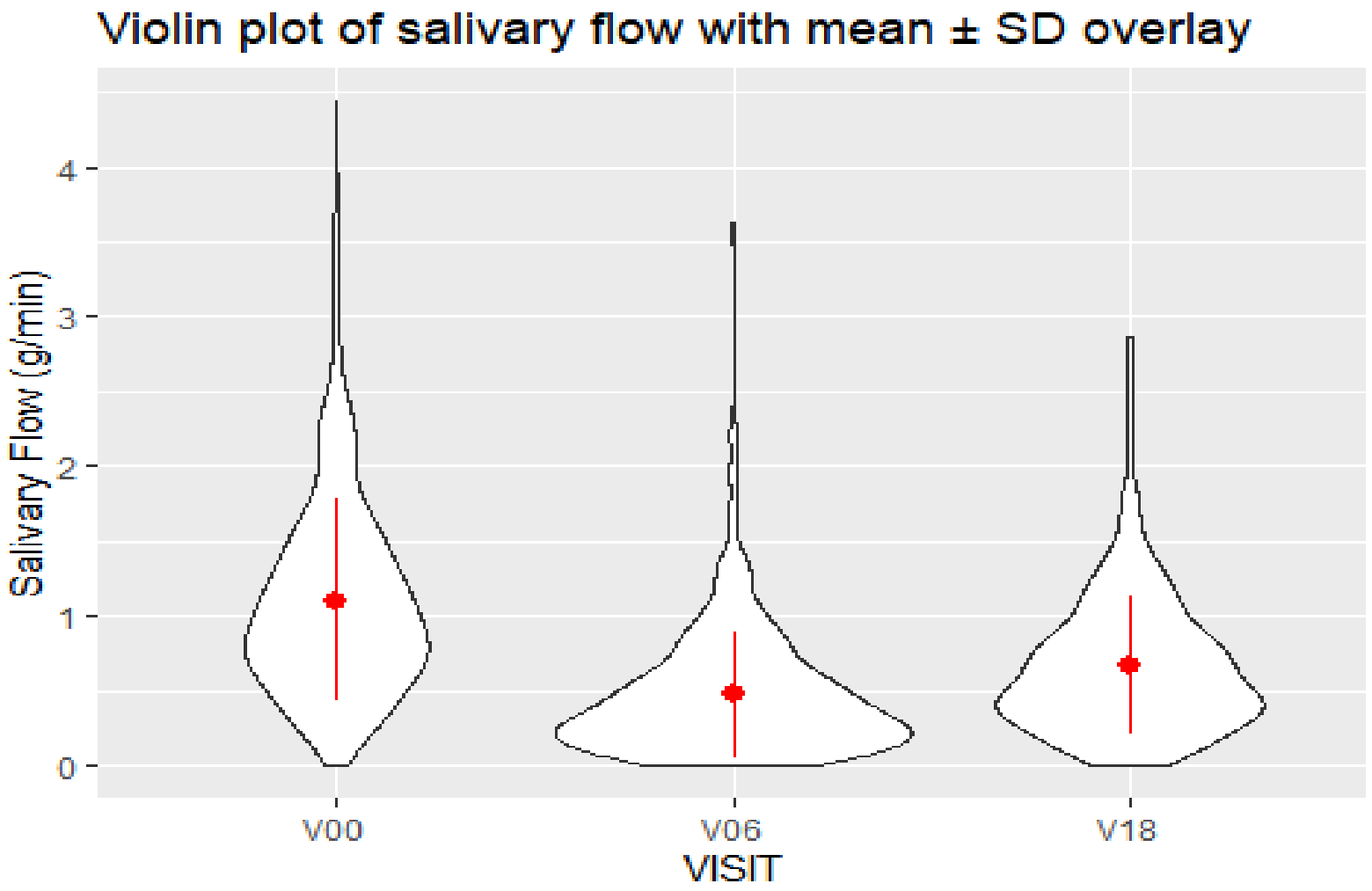
Consultant Meira GTx, Lipella, Afyx Therapeutics


OraRad
Brigham and Women's Hospital
University of Connecticut Health Center
New York University College of Dentistry
University of Pennsylvania School of Dental Medicine
University of North Carolina at Chapel Hill
Atrium Health, Carolinas Medical Center, Charlotte, NC
University of Minnesota, Division of Biostatistics

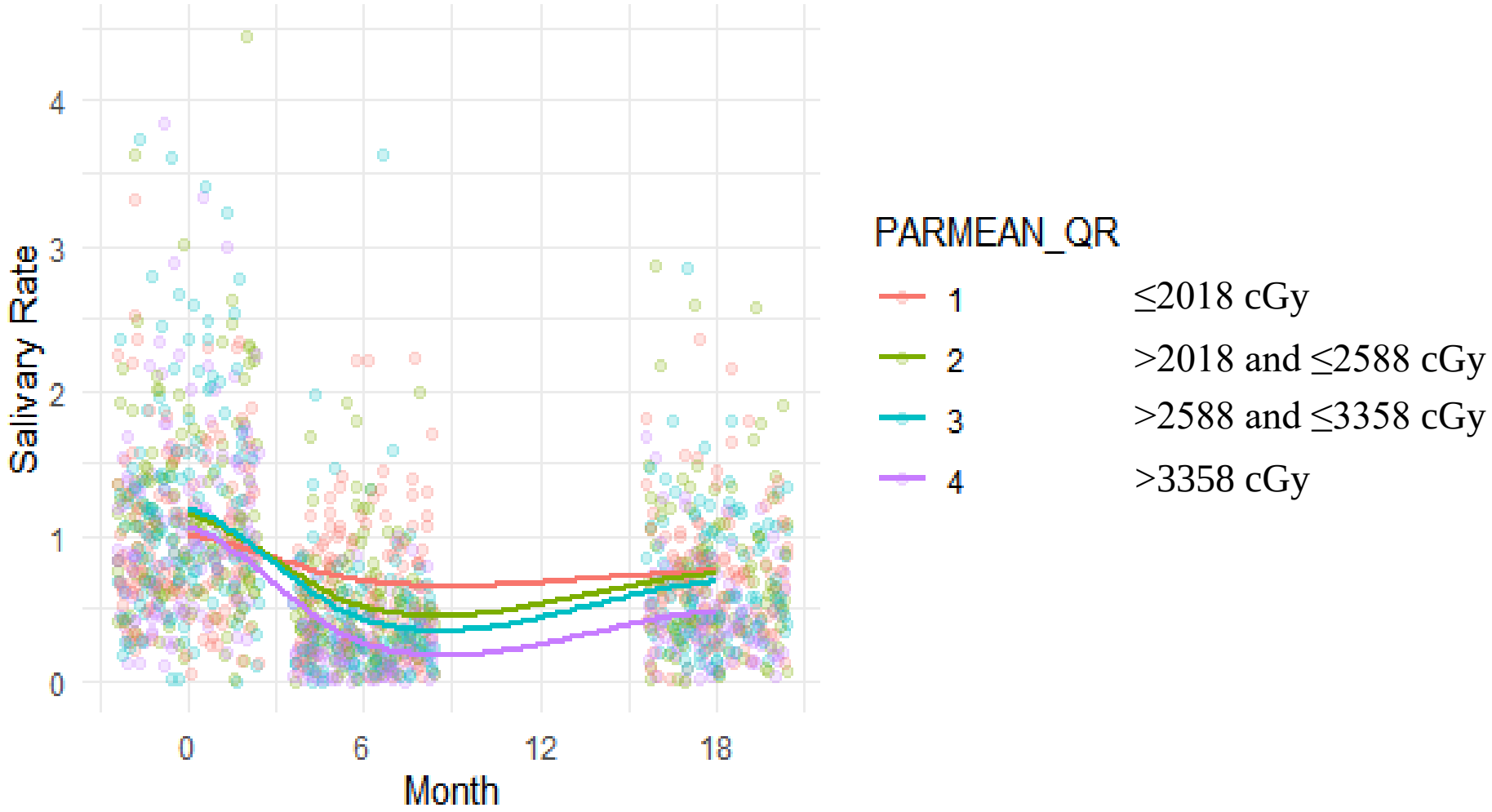
OraRad: Dry Mouth Complaint



OraRad: Salivary Flow



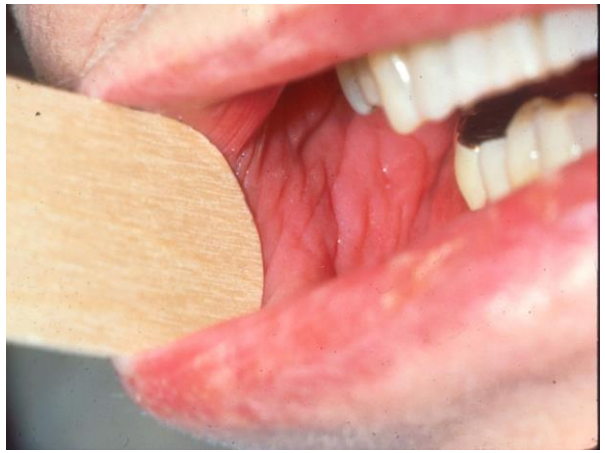
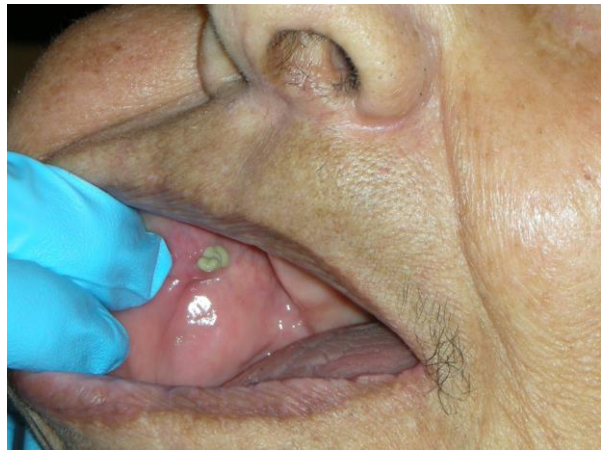
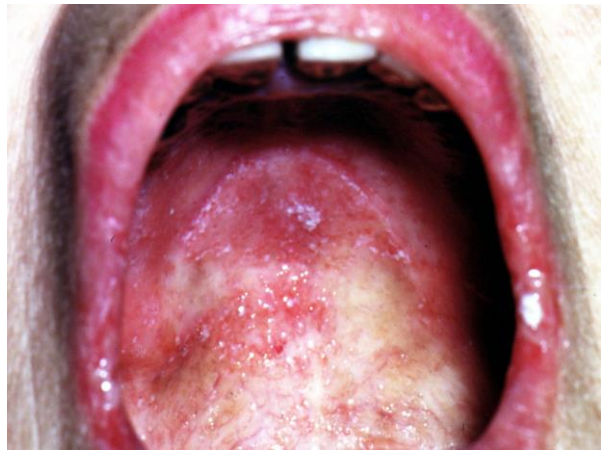
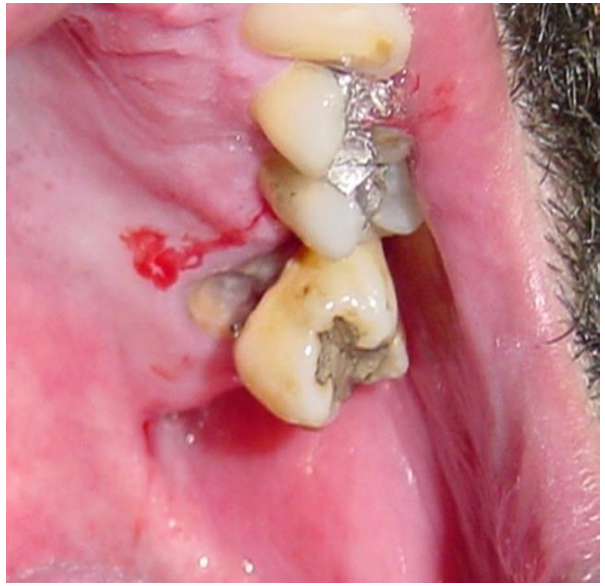
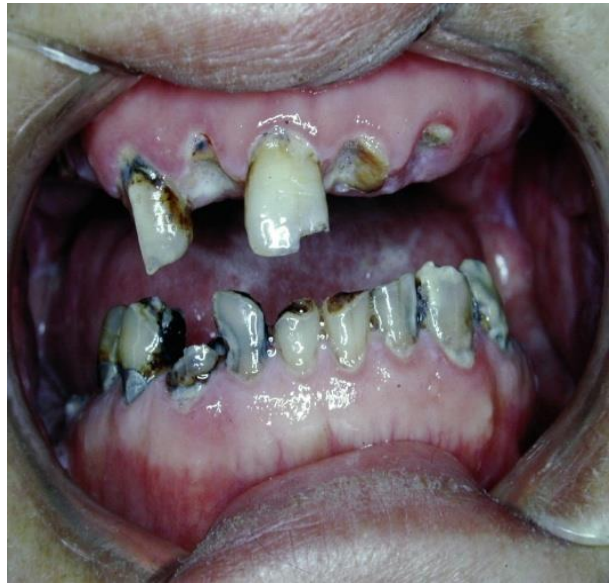
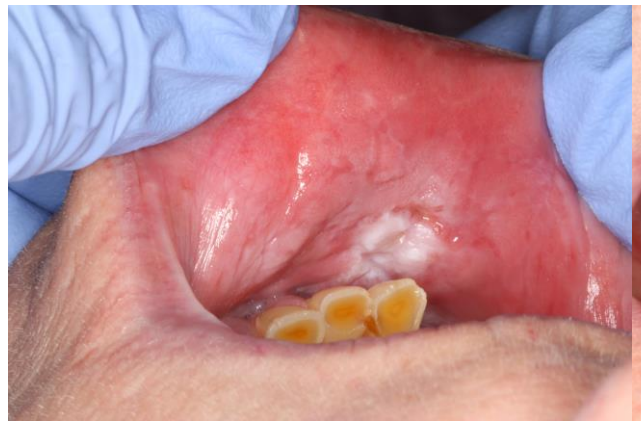
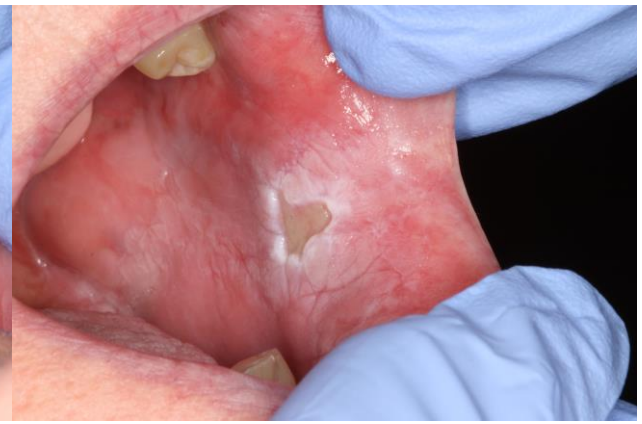
OraRad: Salivary Flow Based on Radiation Quartile



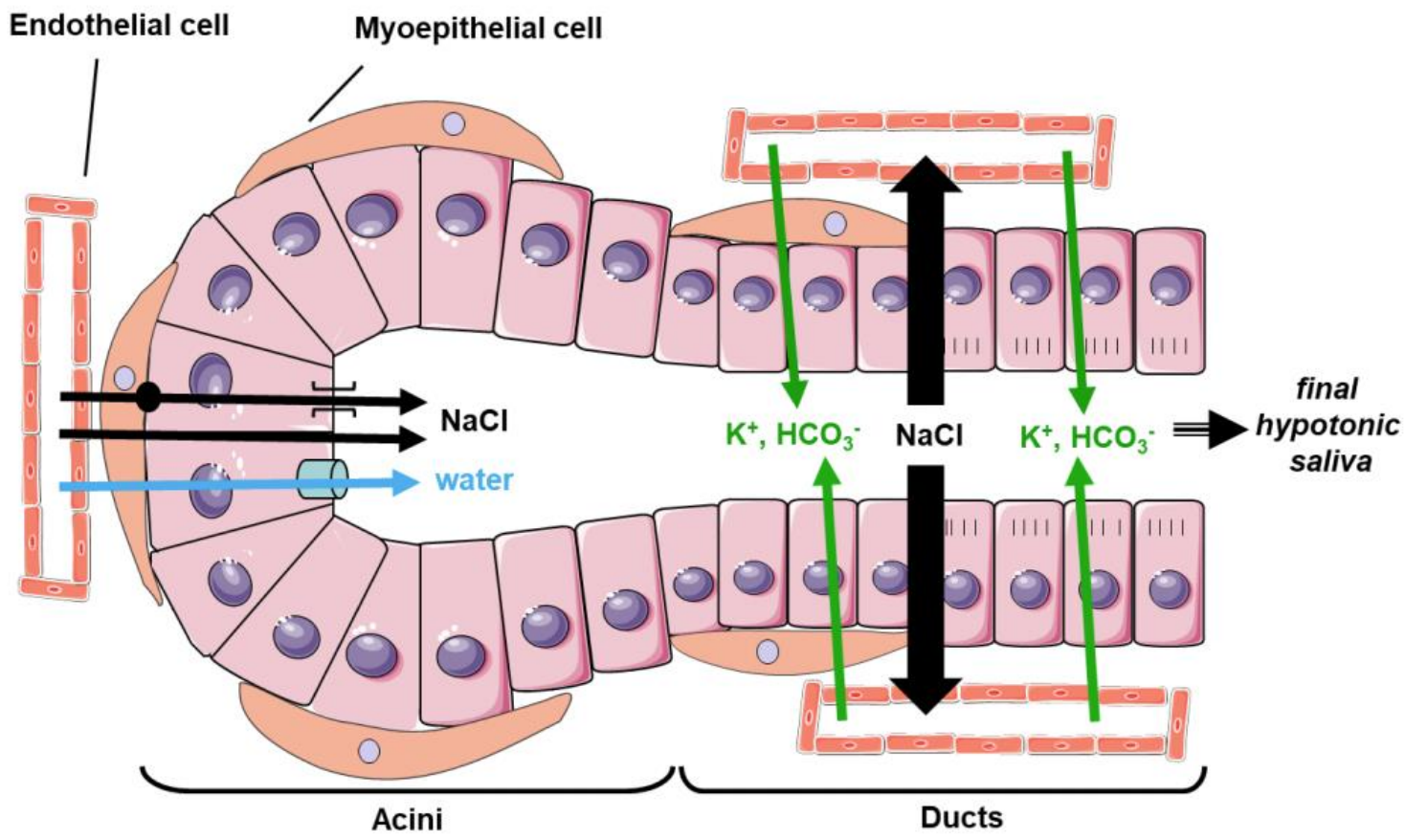
OraRad: Salivary Hypofunction and Subjective Complaints

- Increased patient-reported dysphagia
  - liquids ($p=0.04$)
  - pureed ($p=0.005$)
  - solid foods ($p\leq0.001$)
- Increased problems with taste ($p=0.006$)

Clinical impact of salivary hypofunction

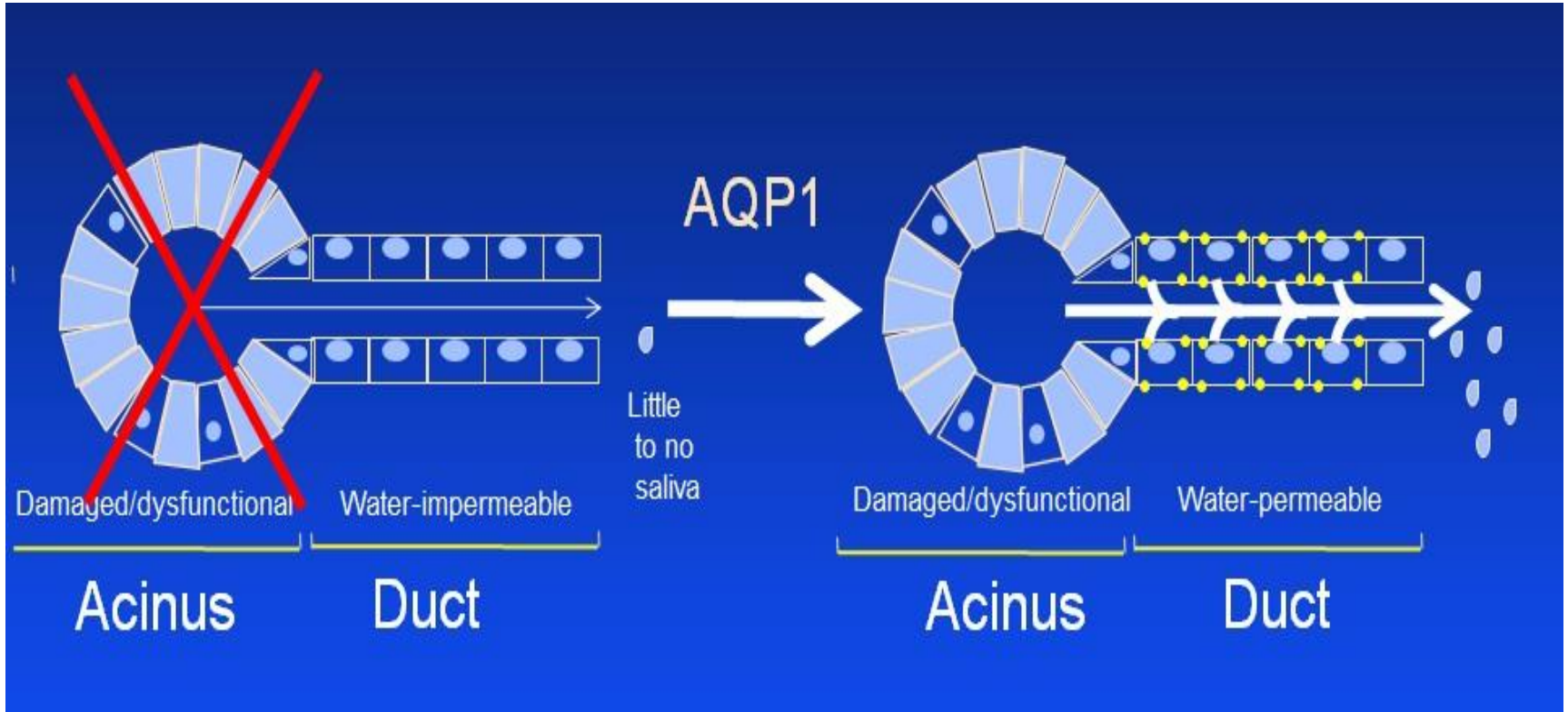
Salivary Gland Function



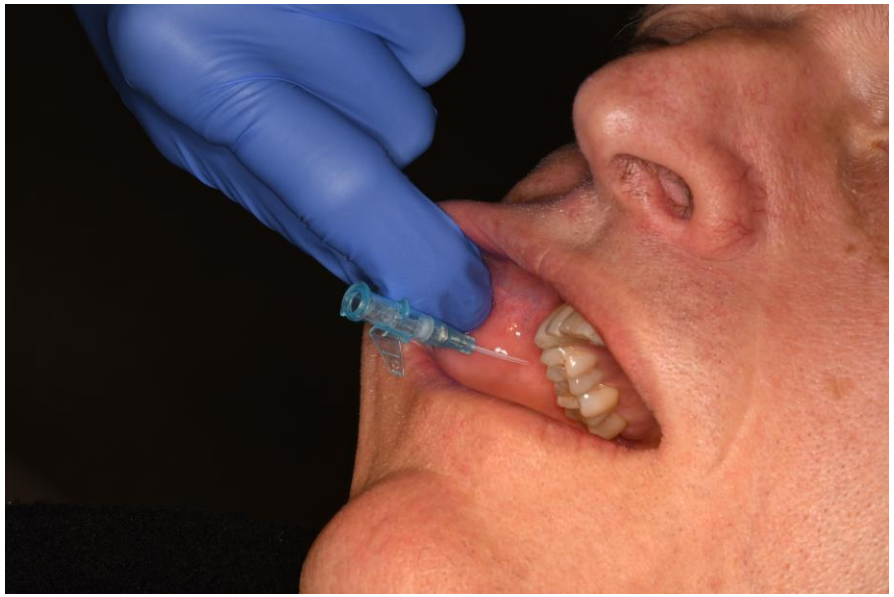
D'Agostino C et al. Insight into Salivary Gland Aquaporins. Cells 2020, 9, 1547

Gene Therapy to Restore Salivary Function

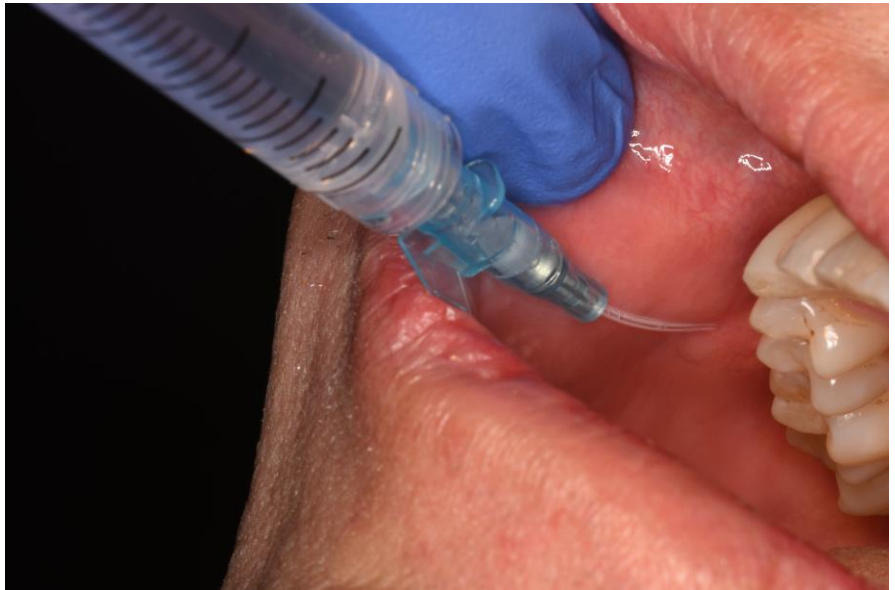
- Introduction of human aquaporin 1 gene (hAQP1) to duct cells via viral vector makes cells permeable to water
- Allows water to flow into the salivary duct and out to the mouth



Delivery of AAV2-hAQP1 – MeiraGTx



- Minimally Invasive
- Local administration
- Well tolerated
- One-time treatment



MGT016 AQUAx Phase 1 Study Design

Study Design

- Open label, multi-center, dose escalation study at 4 sites in USA and Canada
- One-time administration of AAV2-hAQP1 to one (unilateral) or both (bilateral) parotid glands
- Four dose escalating cohorts
- Followed for 1-year post-treatment and then enrolled in long-term 5-year follow-up study

Cohort	Dose
1	1×10^{11} vg/gland (single gland)
2	3×10^{11} vg/gland (single gland)
3	1×10^{12} vg/gland (single gland)
4	3×10^{12} vg/gland (single gland)
1b	3×10^{10} vg/gland (both glands)
2b	1×10^{11} vg/gland (both glands)
3b	3×10^{11} vg/gland (both glands)
4b	1×10^{12} vg/gland (both glands)

MGT016 Outcome Measures

Primary Endpoint

- Safety

Secondary Endpoints

- Patient reported measures of xerostomia symptoms
  - Global Rate of Change Questionnaire (GRCQ)
  - Xerostomia Questionnaire (XQ)
- Whole saliva flow rate

Global Rate of Change Questionnaire (GRCQ)

- Change in Dry Mouth symptoms?
- "Better", "Worse", or "About the Same"
- If "Better" or "Worse": F/U 7-point scale
  - 1 = minimum change
  - 7 = a very important change
- A 2-point change is clinically significant

GLOBAL RATINGS OF CHANGE

1.0 Overall, has there been any change in your **Dry Mouth** since you received study treatment? Please indicate if there has been any change in your **Dry Mouth** by choosing one of the following response options:
(Place an "X" in the appropriate box below)

1. WORSE ☐ *(if **WORSE,** go to question 2.0)*
2. ABOUT THE SAME ☐ *(if **SAME,** go to question 4.0)*
3. BETTER ☐ *(if **BETTER**, go to question 3.0)*

2.0 How much **WORSE** would you say your **Dry Mouth** has been since you received study treatment? Please choose one of the following response options: ***(Record the appropriate response option in the box below)***

1. almost the same, not important
2. a little worse, but large enough to be important
3. somewhat worse, still a small change, but large enough to be important
4. moderately worse, an important change for the worse
5. a good deal worse, an important change for the worse
6. a great deal worse, a very important change for the worse
7. a very great deal worse, a very important change for the worse

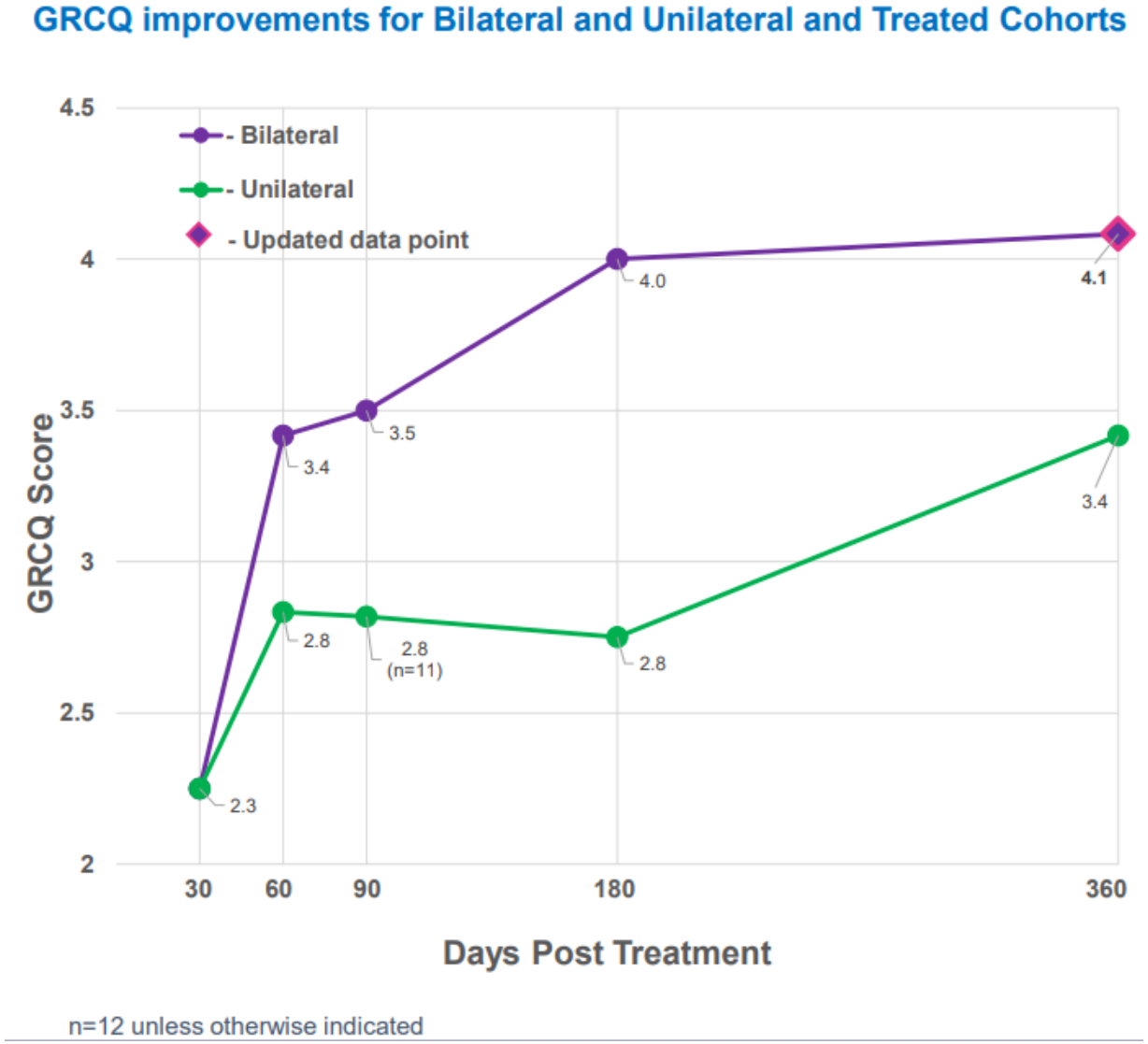
☐ *(go to question 4.0)*

3.0 How much **BETTER** would you say your **Dry Mouth** has been since you received study treatment? Please choose one of the following response options: **(Record the appropriate response option in the box below)**

1. almost the same, not important
2. a little better, but large enough to be important
3. somewhat better, still a small change, but large enough to be important
4. moderately better, an important improvement
5. a good deal better, an important improvement
6. a great deal better, a very important improvement
7. a very great deal better, a very important improvement

☐ *(go to question 4.0)*

GRCQ: Overall Improvement Greater in Bilateral compared to Unilateral treatment group



- GRCQ improvement greater in bilateral vs. unilateral
- Overall improvements were maintained and increased over time in both groups
- Unilateral cohort achieved overall improvement of >3 points at 12 months
- Bilateral cohort overall improvement of >3 points at 2 months and 4 points by 6 months and 12 months

Xerostomia Questionnaire (XQ)

- A Patient Reported Outcome measure
- 8 symptom-specific questions

  0 (not present) to 10 (worst possible)
- Responses are summed (0-80), providing an overall measure of disease burden
- An improvement (decrease) of 8 points (or 10%) or more is considered clinically meaningful

Xerostomia-Specific Questionnaire (XQ)

Objective: To measure patient-reported xerostomia (decreased saliva flow) associated with radiation therapy (RT) for head-and-neck cancer

Instructions: Patients are to rate (circle) each of the eight items on a scale from 0 to 10; the higher the score, the worse the xerostomia

1. Rate your difficulty in talking due to dryness

   0 1 2 3 4 5 6 7 8 9 10
2. Rate your difficulty in chewing due to dryness

   0 1 2 3 4 5 6 7 8 9 10
3. Rate your difficulty in swallowing solid food due to dryness

   0 1 2 3 4 5 6 7 8 9 10
4. Rate the frequency of your sleeping problems due to dryness

   0 1 2 3 4 5 6 7 8 9 10
5. Rate your mouth or throat dryness when eating food

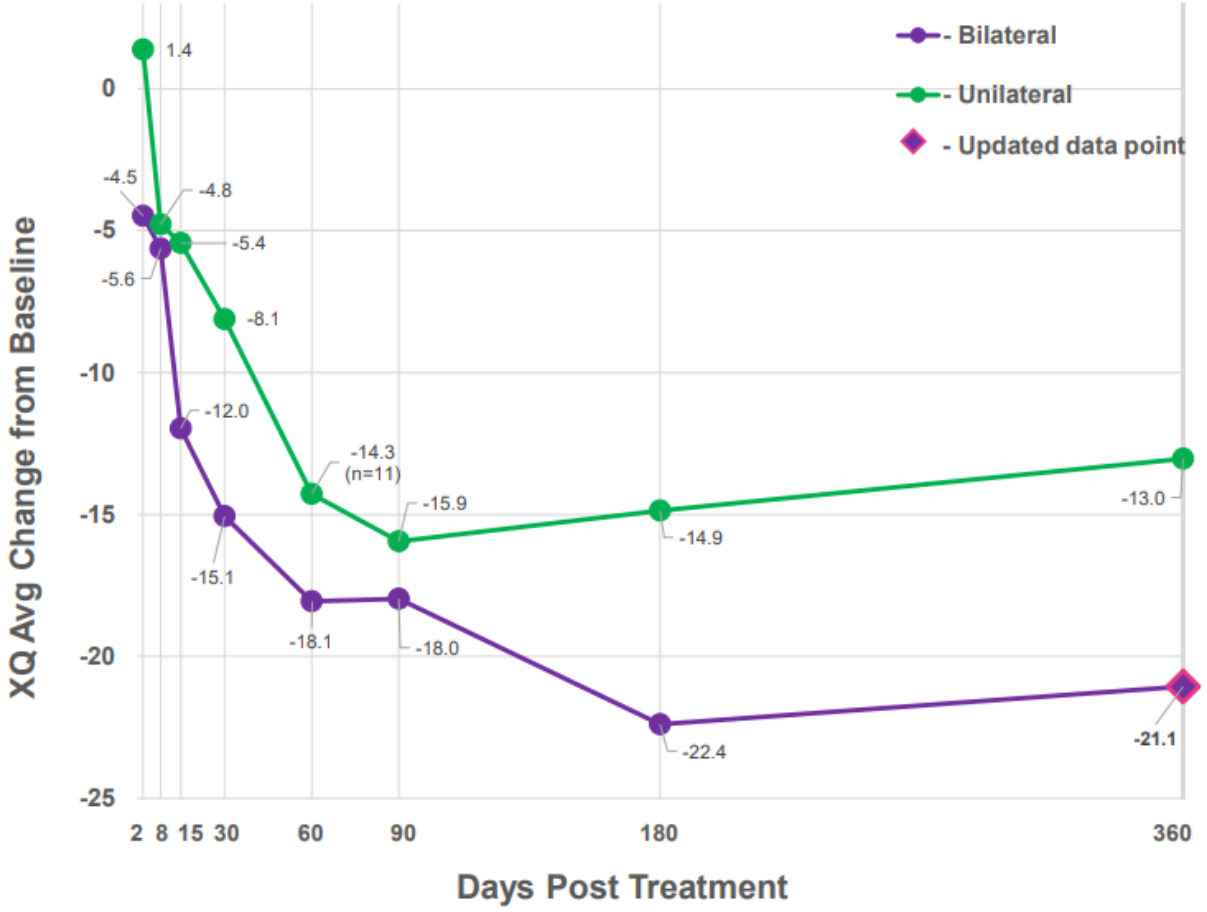
   0 1 2 3 4 5 6 7 8 9 10
6. Rate your mouth or throat dryness while not eating

   0 1 2 3 4 5 6 7 8 9 10
7. Rate the frequency of sipping liquids to aid swallowing food

   0 1 2 3 4 5 6 7 8 9 10
8. Rate the frequency of sipping liquids for oral comfort when not eating

   0 1 2 3 4 5 6 7 8 9 10

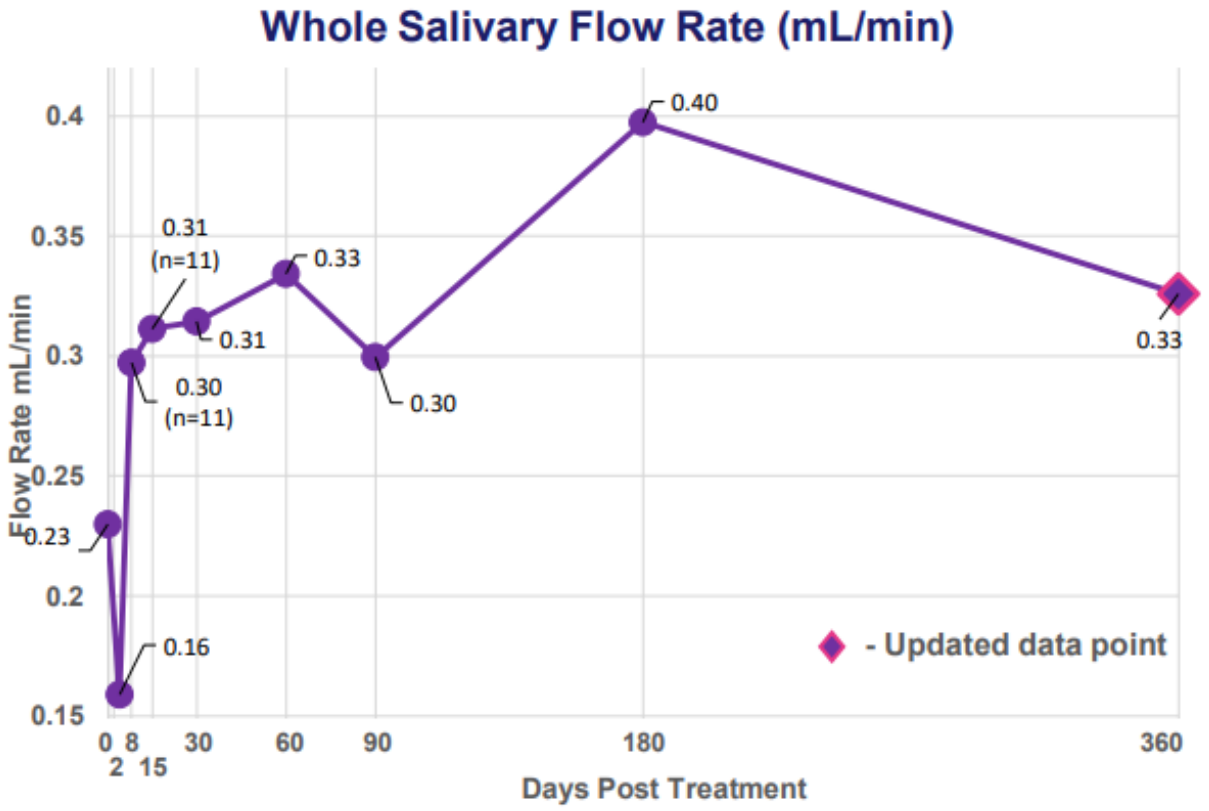
XQ: Substantial Clinically Meaningful Improvements in XQ in both Unilateral and Bilateral treated groups

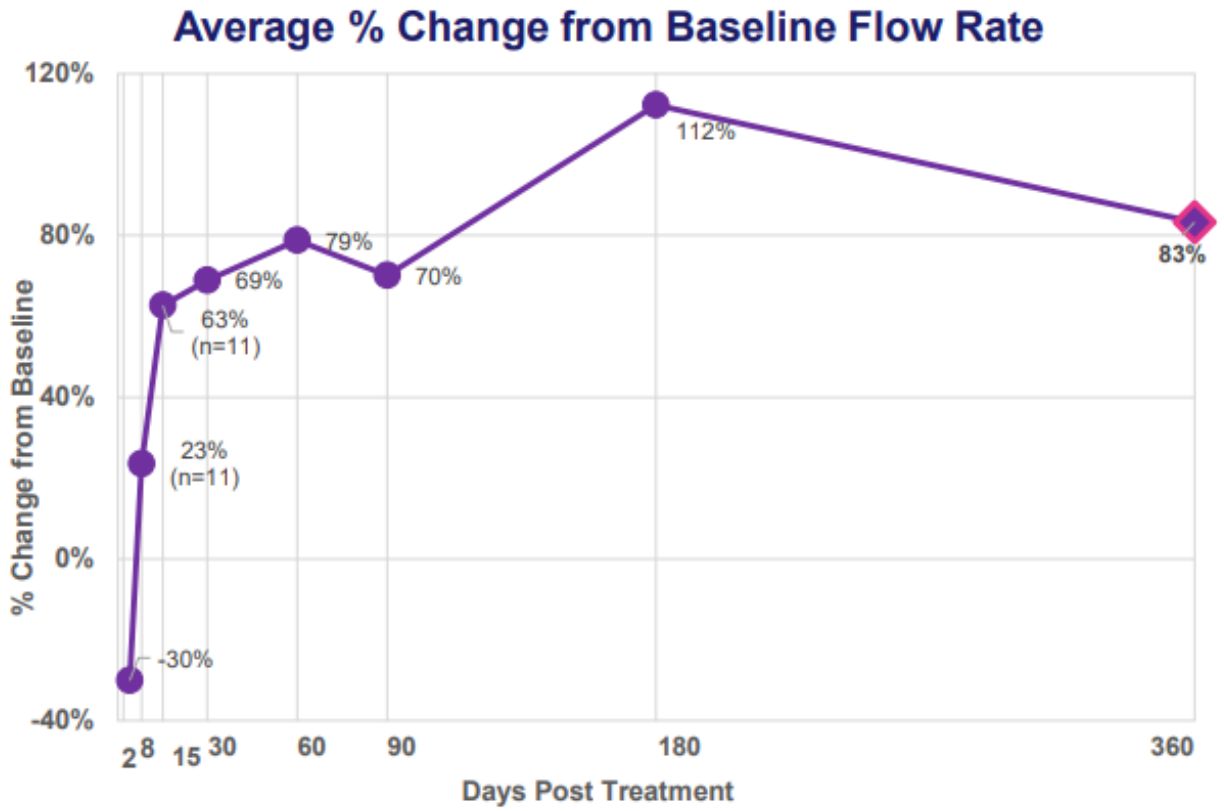


n=12 unless otherwise indicated

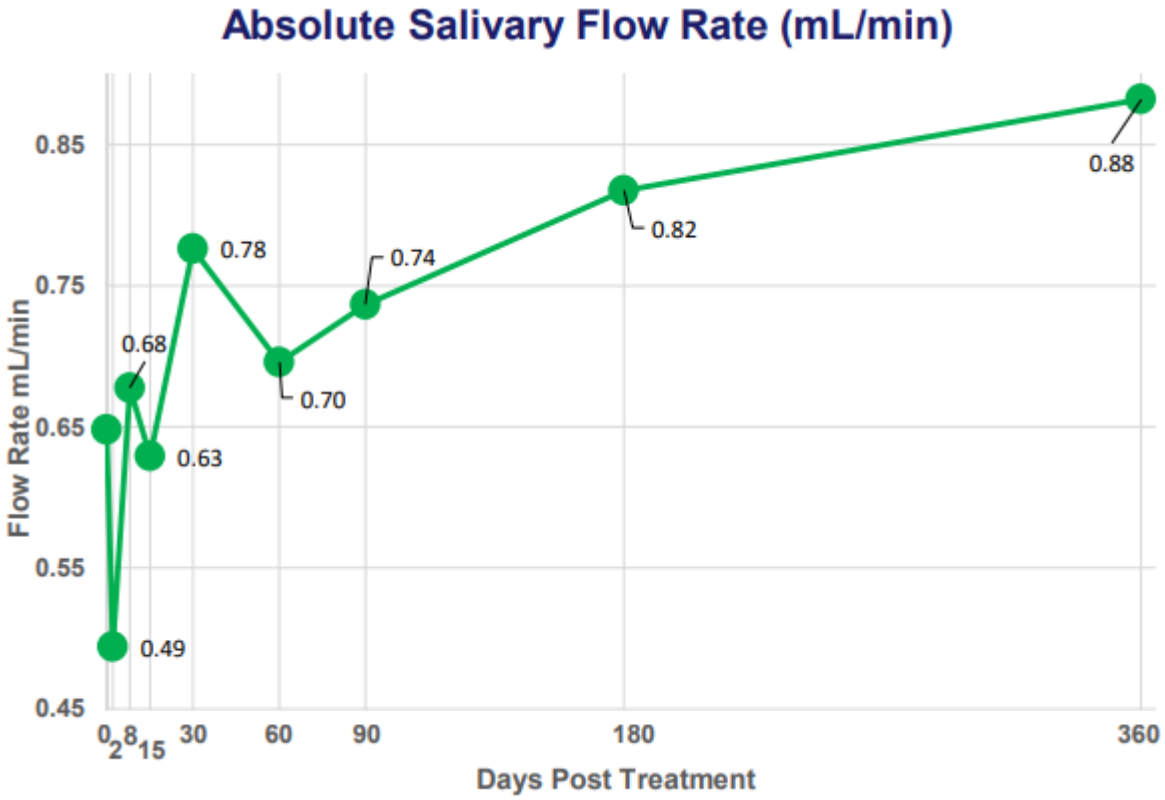
- **Unilateral:** 13-point improvement from baseline at 12 months
- **Bilateral:** 21-point improvement from baseline at 12 months
- Improvement in XQ was observed rapidly post treatment
- In both groups XQ scores improved (declined) >8 points soon after treatment, and >10 points within 2 months after treatment
- As with the GRCQ the degree of improvement was greater in bilateral compared to unilateral treated cohorts

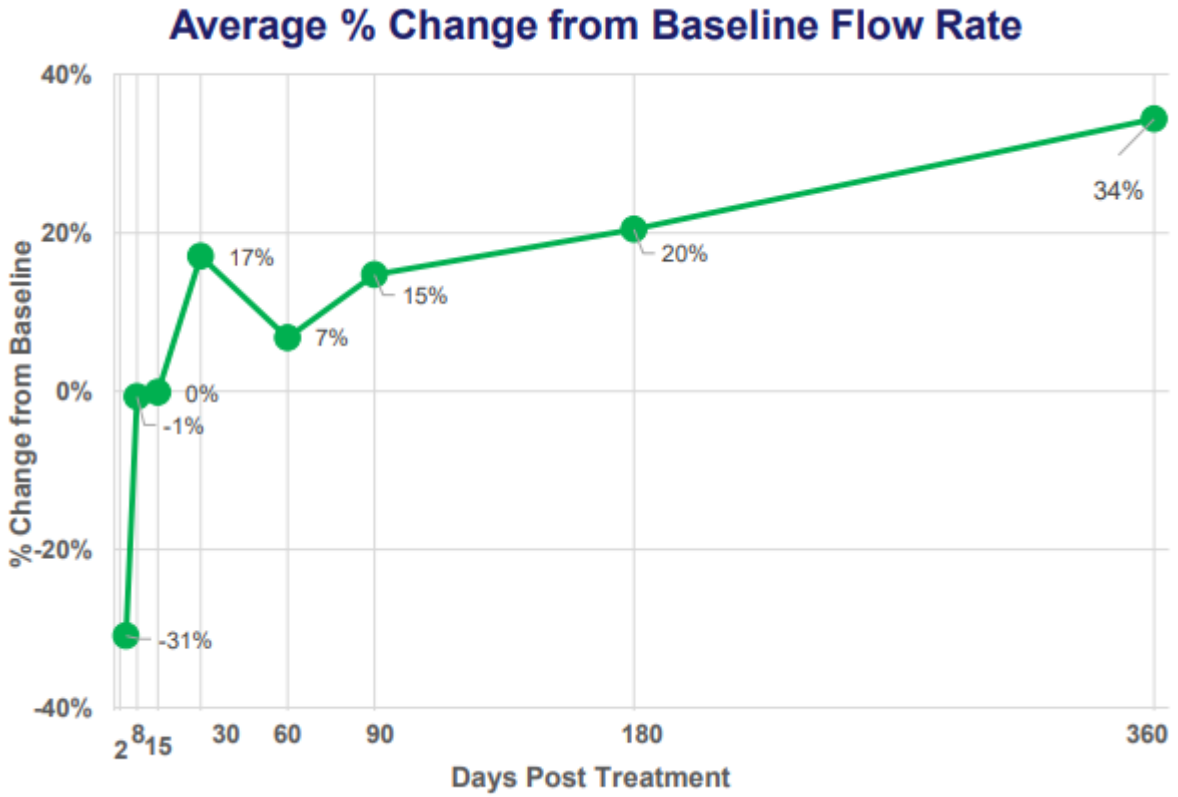
Bilateral Cohorts: Meaningful Improvement in Unstimulated Whole Saliva Production Achieved Reaching Normal Levels Following AAV2-hAQP1 Treatment





Unilateral Treated Subjects Also Showed Improvement in Absolute Whole Saliva Measures (Stimulated)





Future Studies

- Phase II study approved- 20 enrollment sites (n=180)
- Have enrolled the first 2 participants at AH

Acknowledgments- OraRad

NIDCR: Clinical Registry of Dental Outcomes in Head and Neck Cancer Patients (OraRad)(U01DE022939).

- CMC
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- Bruce Baum

Questions?

Mike.Brennan@atriumhealth.org

WAKE FOREST UNIVERSITY SOM FALL RESEARCH SYMPOSIUM 2023

Tricuspid TEER – The Triluminate Study:
A RCT for Tricuspid Regurgitation

Jonathan G. Schwartz, MD, FACC, FSCAI

Medical Director, Interventional Cardiology

Clinical Assistant Professor of Medicine

Sanger Heart & Vascular Institute

Wake Forest University SOM | Atrium Health

Charlotte, NC, USA

TRILUMINATE™ PIVOTAL TRIAL

Wake Forest School of Medicine

Atrium Health Sanger Heart & Vascular Institute

Disclosures

Jonathan G. Schwartz, MD

Consultant, Education, Research support

- Edwards Lifesciences
- Abbott Vascular
- Medtronic, Inc.
- Boston Scientific
- Philips
- Cordis

Advisory Board

- Medtronic, Inc.
- Cordis
- Boston Scientific
- Edwards Lifesciences

Tricuspid Regurgitation

- Tricuspid regurgitation is common, and associated with impaired survival and poor quality of life
- Diuretics are the main therapy, with surgery for selected patients – though often at high operative risk
- Limited data exist in right-sided valvular heart disease, and knowledge is often inferred from left-sided understanding
- Transcatheter tricuspid therapies have recently emerged, but their benefit has not been studied in a randomized, controlled clinical trial

Scientific Objective

- The Triluminate Pivotal Trial is designed to evaluate the safety and effectiveness of transcatheter tricuspid repair with the TriClip™ device in symptomatic patients with severe tricuspid regurgitation who are intermediate or greater estimated risk for mortality with tricuspid valve surgery

Study Leadership

Steering Committee

David Adams	Mount Sinai Hospital
Jörg Hausleiter	Universität München
Patrick McCarthy	Northwestern University
Paul Sorajja	Minneapolis Heart Institute
Raj Makkar	Cedars-Sinai Medical Center
Ralph Stephan von Bardeleben	University Medicine of the Johannes Gutenberg University Mainz
Randolph Martin	Bay Labs, Inc.
Raymond Benza	Ohio State University
Rebecca Hahn	New York-Presbyterian/CUMC
Saibal Kar	Los Robles Medical Center
Scott Lim	University of Virginia Medical Center
Susheel Kodali	New York-Presbyterian/CUMC
Ulrich Jorde	Montefiore Medical Center
Vinod Thourani	Piedmont Hospital

Anatomic Eligibility Committee

Anita Asgar	Montreal Heart Institute
Brian Whisenant	Intermountain Medical Center
Gagan Singh	UC - Davis Medical Center
Gilbert Tang	Mount Sinai Hospital
Hursh Naik	Arizona CV Research Center
M. Azeem Latib	Montefiore Medical Center
Marta Sitges	Hospital Clinic Barcelona
Matthew Price	Scripps Health
Moody Makar	Cedars-Sinai Medical Center
Neil Fam	St. Michael's Hosital
Paul Sorajja	Minneapolis Heart Institute
Philipp Lurz	Universität Leipzig
Ralph Stephan von Bardeleben	University Medicine of the Johannes Gutenberg University Mainz
Rebecca Hahn	New York-Presbyterian/CUMC
Richard Bae	Minneapolis Heart Institute
Saibal Kar	Los Robles Medical Center
Scott Lim	University of Virginia Medical Center
Susheel Kodali	New York-Presbyterian/CUMC
Tom Smith	UC Davis

Patient Management Eligibility Committee

Andrew Sauer	Saint Luke's Health System
Sandhya Murthy	Montefiore Medical Center
Raymond Benza	Ohio State University
Ulrich Jorde	Montefiore Medical Center

Echocardiographic Core Lab

Rebecca Hahn	Cardiovascular Research Foundation
Nadira Hamid	Cardiovascular Research Foundation

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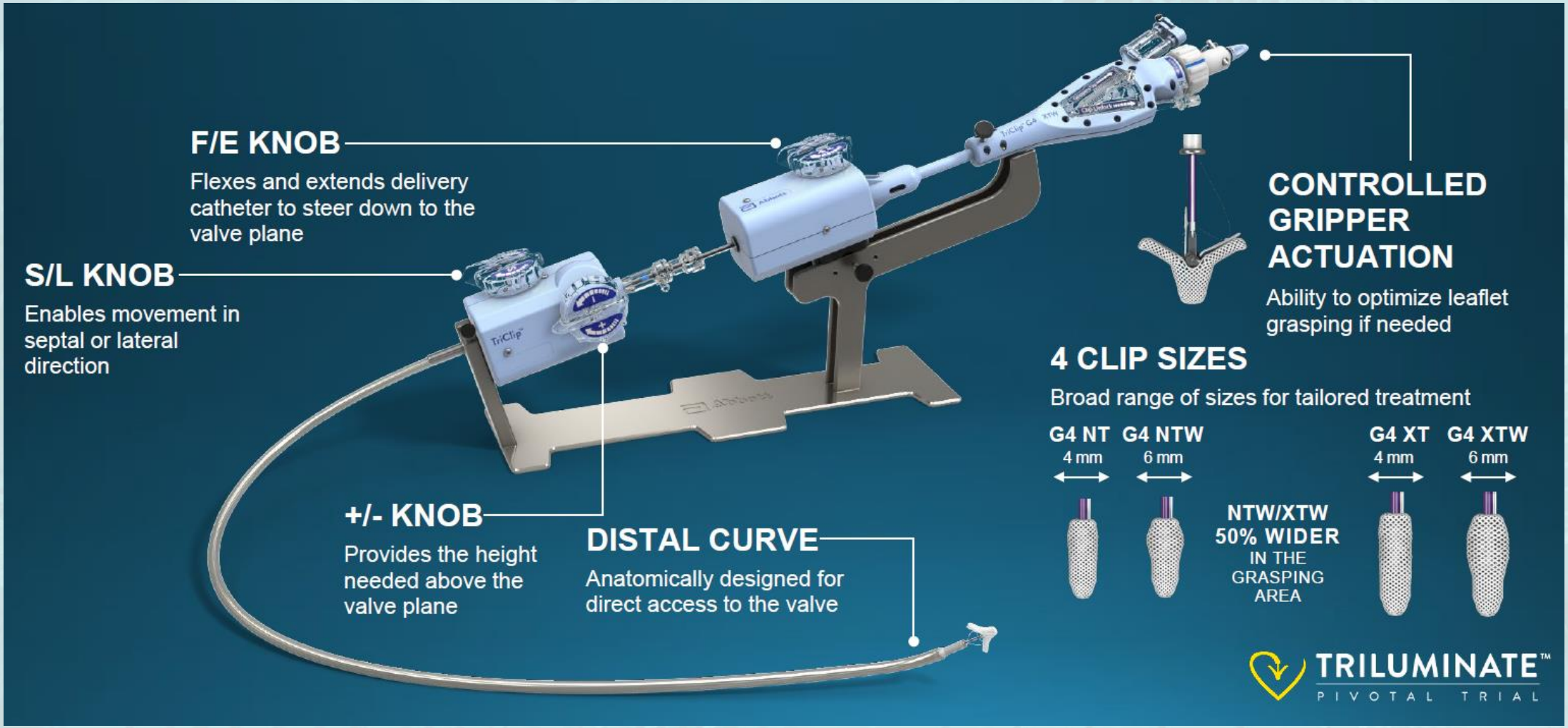
TriClip™ G4 Delivery System



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Study Enrollment Criteria

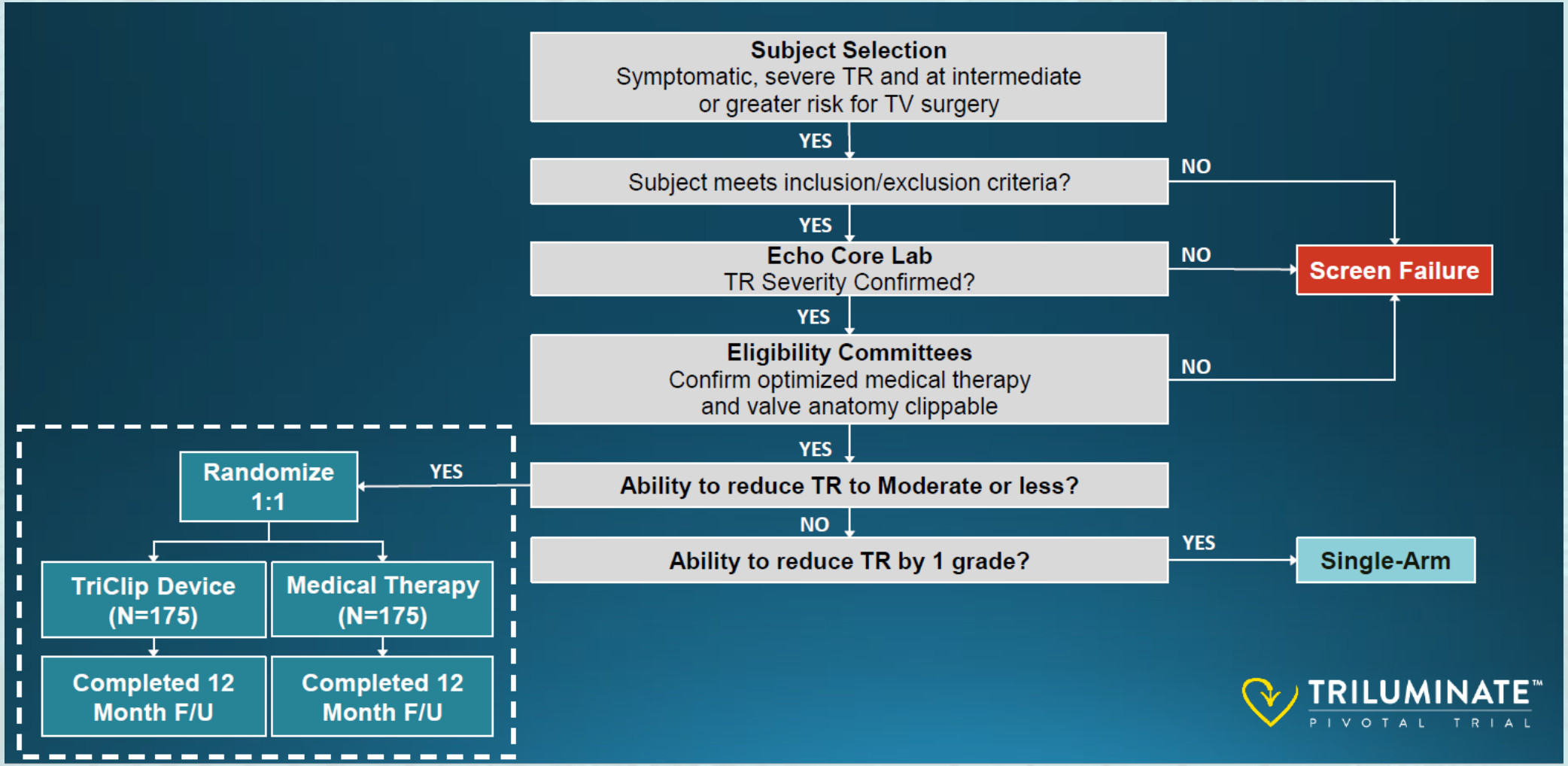
Key Inclusion Criteria

- Severe, symptomatic TR
- Stable GDMT and/or device therapy for heart failure for ≥ 30 days
- ≥ Intermedial risk of mortality/morbidity with tricuspid valve surgery

Key Exclusion Criteria

- Indication for other valve disease intervention
- Severe pulmonary HTN
- Left ventricular ejection fraction ≤ 20%
- Anatomy not suitable for TriClip therapy

Enrollment & Treatment Pathway



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Endpoints & Data Analysis

Trial Design	• Prospective, randomized, controlled, multi-center trial designed to test the superiority of TriClip™ therapy in addition to medical therapy (Device group) over medical therapy alone (Control group) • **450+** subjects enrolled at up to 80 sites in the US, Canada, Europe
Primary Endpoint	**To be assessed after the first 350 randomized subjects complete 12-month follow-up** A composite of mortality or tricuspid valve surgery, heart failure hospitalizations, and quality of life improvement ≥15 points assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ), evaluated at 12 months in a hierarchical fashion using the Finkelstein-Schoenfeld methodology
Secondary Endpoint	**Assessed hierarchically in the following order:** • Freedom from major adverse events (MAE) after procedure attempt (femoral vein puncture) at 30 days (Device group only) • Change in KCCQ at 12 months (superiority of Device vs. Control) • TR Reduction to moderate or less at 30-day post procedure (superiority of Device vs. Control) • Change in 6MWD at 12 months (superiority of Device vs. Control)

MAE defined as composite of cardiovascular mortality, new onset renal failure, endocarditis requiring surgery, and non-elective cardiovascular surgery for TriClip device-related AE post-index procedure

Global Geographical Participation

- Abbott Northwestern Hospital
- Allegheny General Hospital- ASRI
- Arizona Cardiovascular Research Center
- Aurora Medical Group
- Austin Heart
- Baptist Hospital of Miami
- Baylor Scott & White Heart & Vascular Hospital
- Beth Israel Deaconess Medical Center
- Brigham & Women's Hospital
- Buffalo General Hospital
- California Pacific Medical Center - Van Ness Campus
- Cardiovascular Institute of the South
- Cardiovascular Research Institute of Kansas
- Carolinas Medical Center
- Cedars-Sinai Medical Center
- Centennial Heart Cardiovascular Consultants
- Christ Hospital
- El Camino Hospital
- Hospital of the University of Pennsylvania
- Inova Fairfax Hospital
- Intermountain Medical Center
- JFK Medical Center
- Kansas University Medical Center
- Los Robles Regional Medical Center
- Manatee Memorial Hospital
- MedStar Health Research Institute
- Methodist Hospital of San Antonio
- Montefiore Medical Center - Moses Division
- Morton Plant Valve Clinic
- Mount Sinai Hospital
- New York-Presbyterian/Columbia University Medical Center
- North Shore University Hospital
- Northshore University HealthSystem
- Novant Health Heart and Vascular Research Institute
- Ohio Health Research Institute
- Phoenix Cardiovascular Research Group
- Piedmont Heart Institute
- Providence Heart & Vascular Institute
- Providence Medical Foundation
- Rush University Medical Center
- Scripps Health
- Sentara Norfolk General Hospital
- St. Thomas Hospital
- Sutter Medical Center, Sacramento
- Swedish Medical Center
- Tallahassee Research Institute
- The Cleveland Clinic Foundation
- The Methodist Hospital
- Tucson Medical Center
- University Hospital - Univ. of Alabama at Birmingham (UAB)
- University of California - Davis Medical Center
- University of Colorado Hospital
- University of Pittsburgh Medical Center
- University of Virginia Medical Center
- Yale New Haven Hospital
- Hamilton Health Science Centre
- Herzzentrum Leipzig GmbH
- Hospital Clínic de Barcelona
- Institut de Cardiologie de Montreal (Montreal Heart Inst.)
- Munchen Grosshadern
- Ospedale San Raffaele - Cardiac
- Ottawa Heart Institute
- St. Michael's Hospital
- St. Paul's Hospital
- Sunnybrook Health Sciences Centre
- Universitatsklinikum Bonn AdoR
- Universitatsmedizin der Johannes Gutenberg-Universitat Mainz

TRILUMINATE™ PIVOTAL TRIAL

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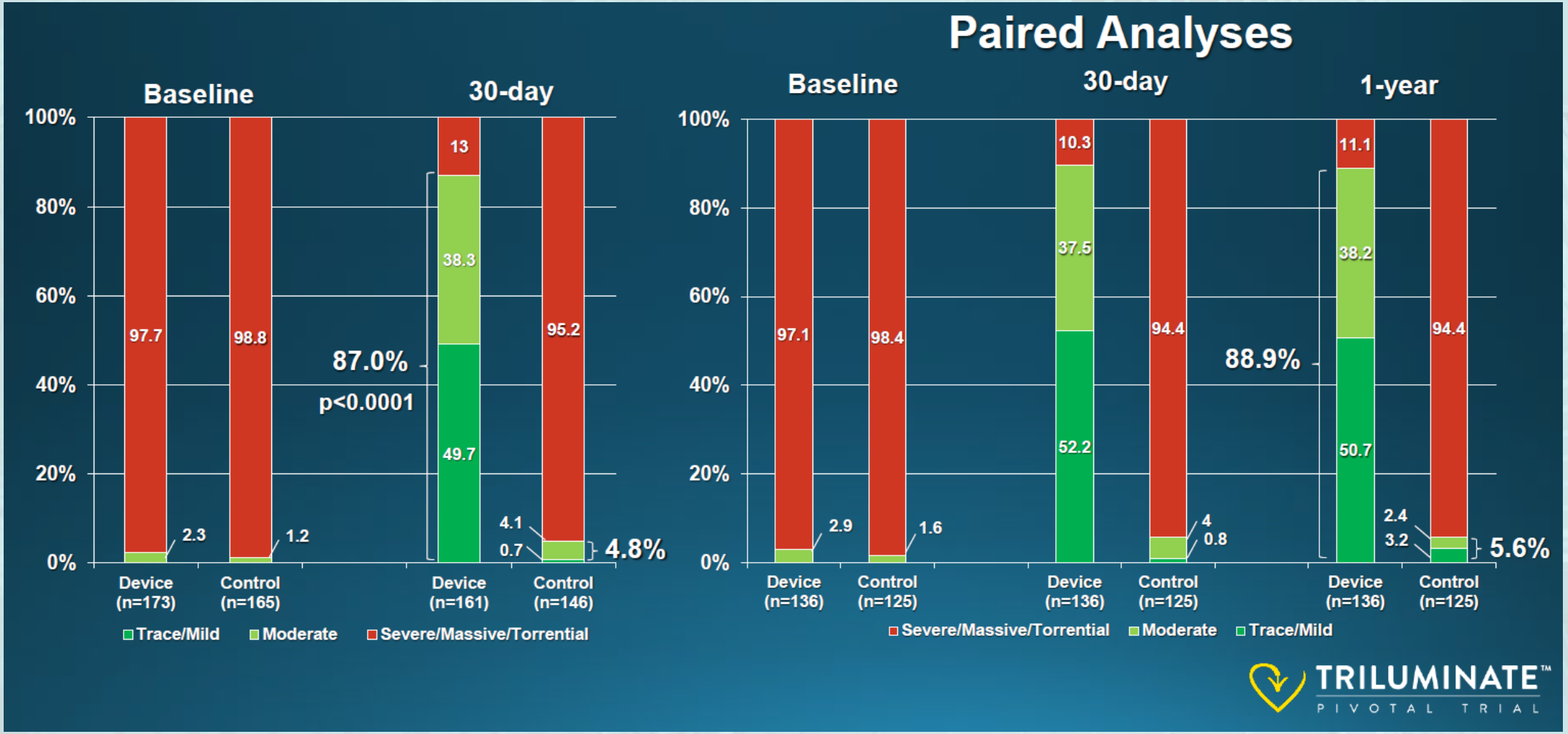
Baseline Characteristics

	Device N=175 # (%)	Control N=175 # (%)
Age, Mean (years)	78.0 ± 7.4	77.8 ± 7.2
Sex (Female)	98 (56.0)	94 (53.7)
NYHA class III or IV	104 (59.4)	97 (55.4)
KCCQ Score, mean	56.0 ± 23.4	54.1 ± 24.2
Hypertension	142 (81.1)	141 (80.6)
Renal disease	62 (35.4)	62 (35.4)
Liver disease	11 (6.3)	16 (9.1)
Atrial fibrillation	153 (87.4)	162 (92.6)
Diabetes	28 (16.0)	27 (15.4)
COPD	19 (10.9)	24 (13.7)
CRT/CRT-D/ICD/PPM	28 (16.0)	24 (13.7)
Prior aortic intervention	27 (15.4)	27 (15.4)
Prior mitral intervention	45 (25.7)	42 (24.0)
Prior tricuspid intervention	1 (0.6)	0 (0.0)

	Device N=175 # (%)	Control N=175 # (%)
TR Severity		
Moderate	4 (2.3)	2 (1.2)
Severe	44 (25.4)	49 (29.7)
Massive	37 (21.4)	30 (18.2)
Torrential	88 (50.9)	84 (50.9)
Etiology (functional)	165 (94.8)	158 (92.9)
Coaptation Gap, Mean (mm)	5.5 ± 1.8	5.2 ± 1.7
Heart size/function, Mean		
RVEDD (base, cm)	5.0 ± 0.8	5.2 ± 0.8
TV annulus diameter (cm)	4.3 ± 0.7	4.5 ± 0.8
RV TAPSE (cm)	1.7 ± 0.4	1.6 ± 0.4
LVEF (%)	59.3 ± 9.3	58.7 ± 10.5
CO (L/min)	4.1 ± 1.2	4.2 ± 1.1

Reduction in TR Severity



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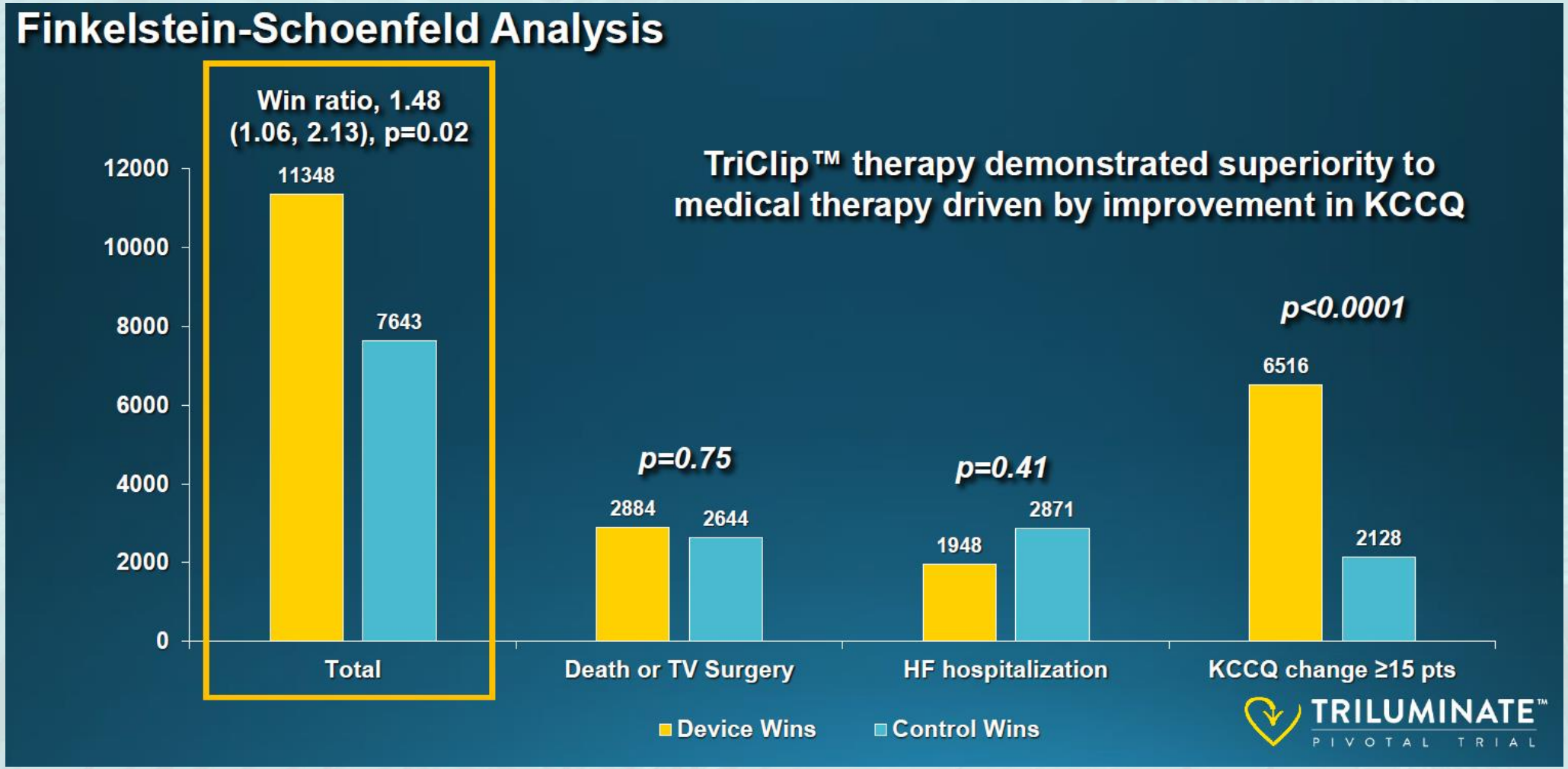
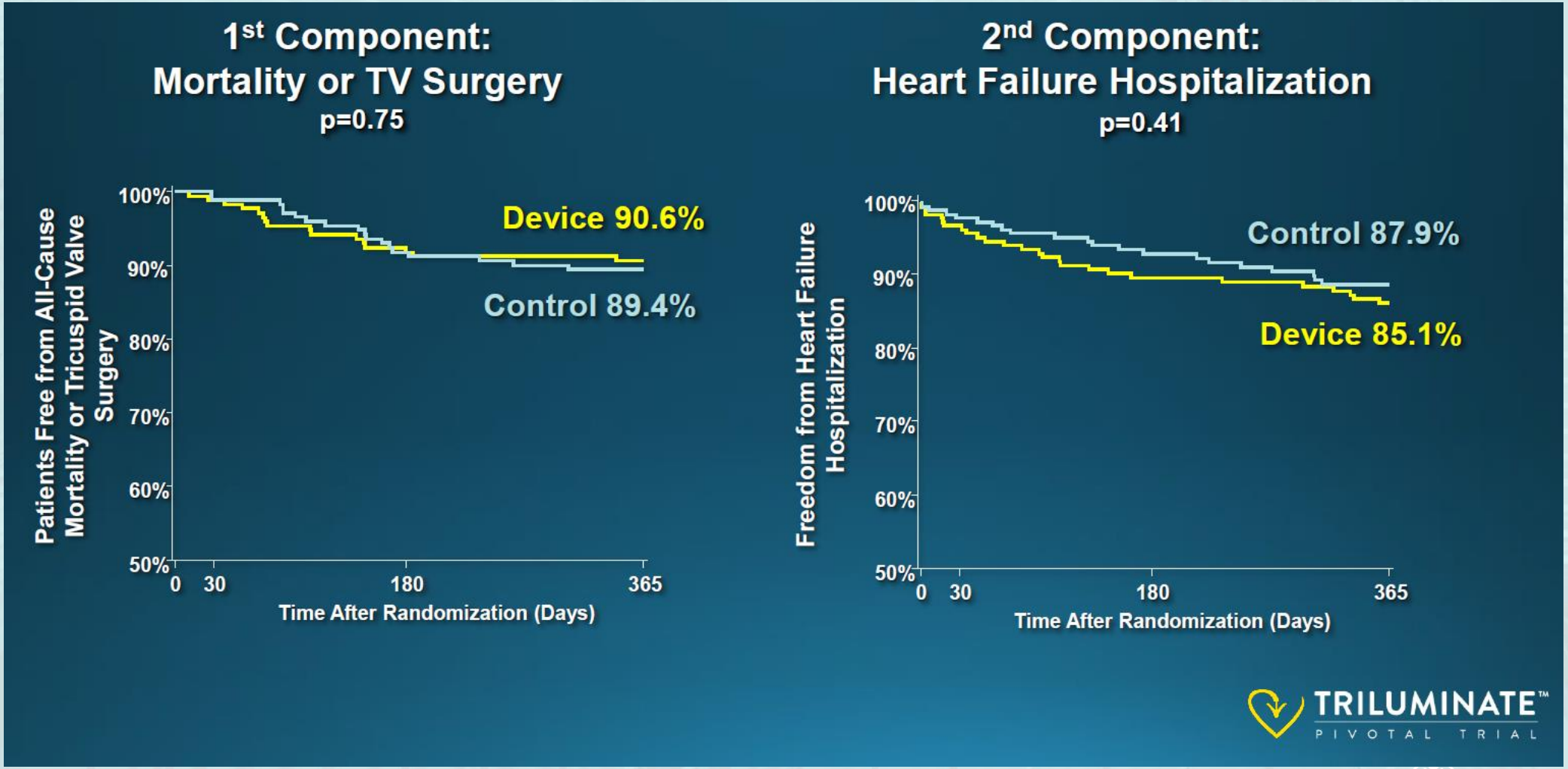
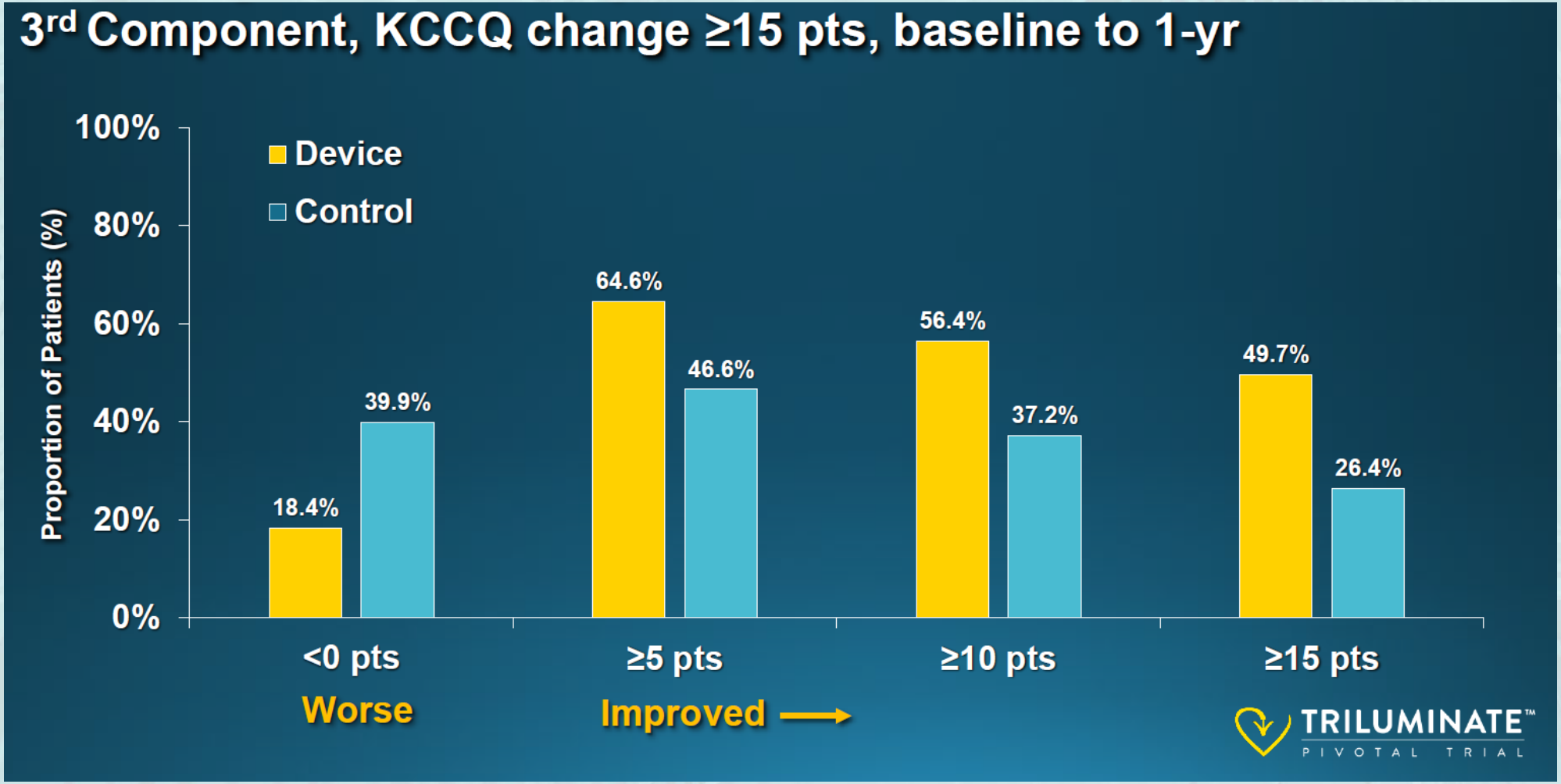
Primary Endpoint



Individual Component Analysis



Quality of Life Improvement



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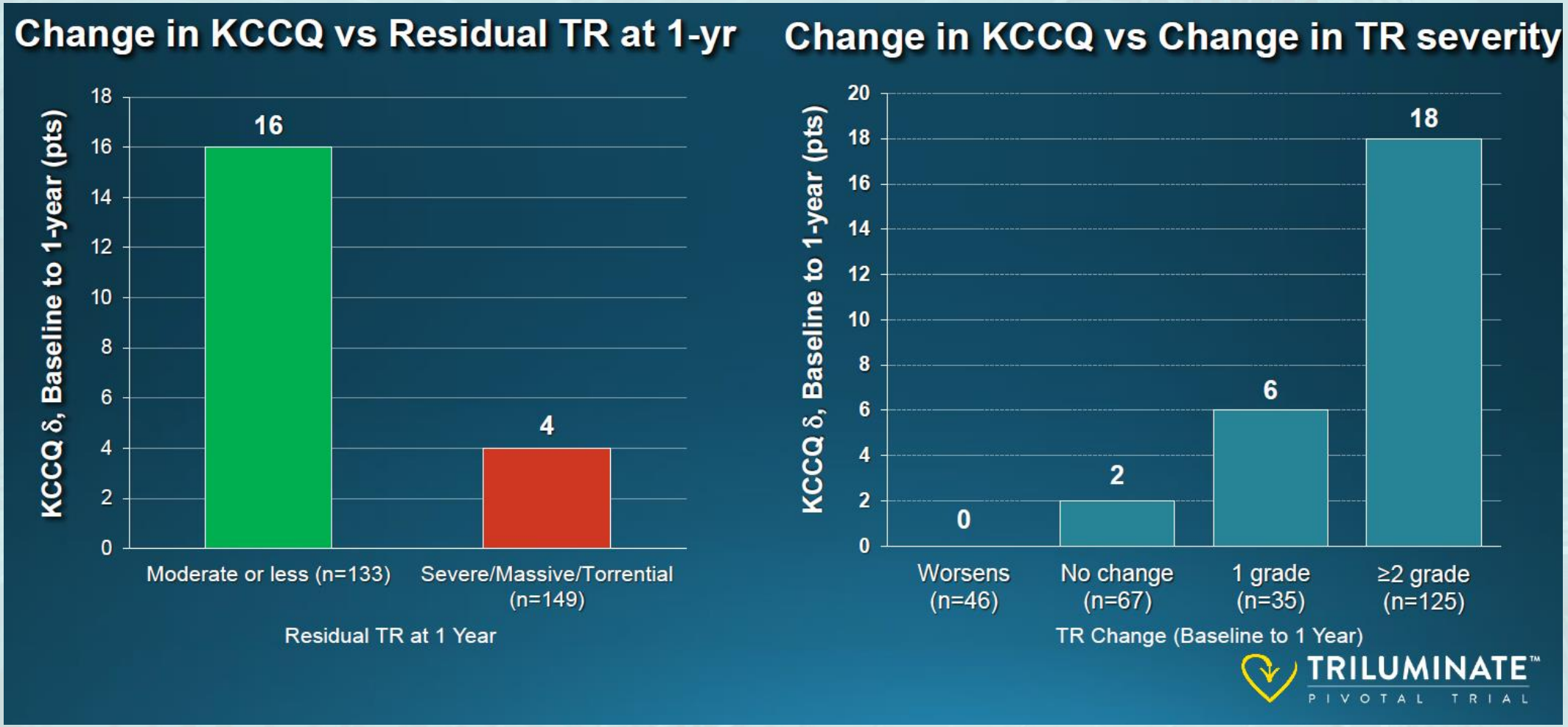
Relationship between TR and QOL



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Hierarchical Secondary Endpoints

	Device Group (N=175)	Control Group (N=175)	Difference (95% CI)	p-value
Freedom from MAE through 30 Days post procedure – Kaplan-Meier estimate of event-free rate (lower 97.5% CI)[1]	98.3	-	-	<0.001
Change in KCCQ from baseline to 12 months (pts)[2]				
Endpoint analysis	12.3	0.6	11.7	<0.001
Non-imputed data	15.2	4.8	10.4	-
TR Severity ≤ Moderate at 30 Days – no./total no (%)	87.0	4.8	-	<0.001
Change in 6-min walk test distance from baseline to 12 months (m)[2]				
Endpoint analysis	-8.1	-25.2	17.1	0.25
Non-imputed data	11.5	-8.7	20.3	-

[1]MAE performance goal 90%
[2]Subjects who experienced a HF-related CV death or received tricuspid valve surgery had KCCQ score and 6MWT distance imputed as 0 at 12 months. 6MWT also imputed as 0 for subjects unable to exercise due to cardiac reasons.

Safety Profile

Major Adverse Event (MAE) Through 30 Days Post-Procedure – no.(%)	Device N=172†
Total	**3 (1.7%)**
Cardiovascular mortality	1 (0.6%)
Endocarditis requiring surgery	0 (0%)
New-onset renal failure	2 (1.2%)
Non-elective CV Surgery, TVRS for device-related AE	0 (0%)

Other Clinical Safety Endpoints Through 30 Days Post-Procedure– no.(%)	Device N=172†
Any-cause mortality	1 (0.6%)
Tricuspid valve surgery	1 (0.6%)
Tricuspid valve re-intervention	3 (1.7%)
Major bleeding#	8 (4.7%)
Tricuspid mean gradient ≥ 5mmHg	8 (4.7%)
Single leaflet device attachment (SLDA)*	12 (7.0%)
Stroke	1 (0.6%)
Myocardial Infarction	0 (0%)
Embolization*	0 (0%)
Thrombosis	0 (0%)
New CRT/CRT-D/ICD/perm. pacemaker^	1 (0.6%)

†Attemptd procedure population (3 subjects randomized to device withdrew consent prior to index procedure)
#Defined as bleeding ≥ Type 3 based on modified BARC definition
*SLDA and embolization evaluated though 30-day follow-up
^Assessed through adverse event reporting

Limitations

- Since patients were not blinded, a Hawthorne effect may have played a role in outcomes in both groups
- The trial was conducted almost entirely during the COVID-19 pandemic, which may have affected clinical outcomes

Summary

- TR was reduced by TriClip therapy to moderate or less in 87%, vs. only 4.8% for the control group, and the reduction was sustained to 1-year follow-up
- The primary endpoint was met (p=0.02) demonstrating device superiority, driven mainly by significant improvement in QOL
- Degree of TR reduction was related to degree of improvement in QOL
- The 30-day MAE rate was only 1.7%, and death and pacemaker implant each occurred in 0.6%
- Survival free of mortality and TV surgery was high at 1 year in both groups (~90%)

Conclusions

- Triluminate Pivotal is a pioneering study as the first RCT in this unique population of patients with severe TR
- The TriClip device was highly effective in reducing TR and led to significant improvements in QOL at 1 year, without the high procedural risk often associated with tricuspid surgery
- These results are very meaningful for a highly symptomatic population whose QOL is impacted by TR
- With the excellent benefit-to-risk profile of the TriClip system, a historically untreated population will have a treatment option to improve their QOL

Manuscript

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Repair for Patients with Tricuspid Regurgitation

Paul Sorajja, M.D., Brian Whisenant, M.D., Nadira Hamid, M.D., Hursh Naik, M.D., Raj Makkar, M.D., Peter Tadros, M.D., Matthew Price, M.D., Gagan Singh, M.D., Neil Fam, M.D., Saibal Kar, M.D., Jonathan G. Schwartz, M.D., Shamir Mehta, M.D., Richard Bae, M.D., Nishant Sekaran, M.D., Travis Warner, M.D., Moody Makar, M.D., George Zorn, M.D., Erin Spinner, Ph.D., Phillip M. Trusty, Ph.D., Raymond Benza, M.D., Ulrich Jorde, M.D., Patrick McCarthy, M.D., Vinod Thourani, M.D., Gilbert H.L. Tang, M.D., Rebecca Hahn, M.D., and David H. Adams, M.D., for the TRILUMINATE Investigators*

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- Sanger Structural Heart Imaging: Dr. Markus Scherer, Dr. Noreen Kelly
- Sanger clinical research team
- Cat Shah, NP; Amanda Wilson, RN
- Cath lab teammates + leadership
- Patients

Wake Forest School of Medicine

Atrium Health

Sanger Heart & Vascular Institute

Atrium Health
Sanger Heart & Vascular Institute

@jgschwartzmd
jonathan.schwartz@atriumhealth.org
704.456.5133

Patient Engagement, Attrition, and Missed Appointments

JOSEPH "JOEY" SKELTON, MD, MS
DEPARTMENT OF PEDIATRICS

Wake Forest University
School of Medicine

The academic core of Atrium Health

Background: Attrition from obesity treatment

- Clinical Programs: few studies
  - 6 with focus on attrition (reports or retrospective)
  - 4 with attrition as secondary outcome
  - 27 to 73% attrition rate reported
- Clinical Trials: little difference compared to clinical programs
  - Overall: 18-33%
  - 83% in one arm- re-randomized
  - Cochrane Review 2009: 0-42%

obesity reviews doi: 10.1111/j.1467-789X.2010.00803.x

Obesity Management

Attrition in paediatric weight management: a review of the literature and new directions

J. A. Skelton[1,2] and B. M. Beech[1,3]

[1]Department of Pediatrics, Wake Forest University School of Medicine, Winston-Salem, NC, USA; [2]Brenner FIT Program, Brenner Children's Hospital, Winston-Salem, NC, USA; [3]Department of Social Sciences and Health Policy, Division of Public Health Sciences, Department of Pediatrics, Wake Forest University School of Medicine, Winston-Salem, NC, USA

Received 6 May 2010; revised 14 July 2010; accepted 4 August 2010

Summary

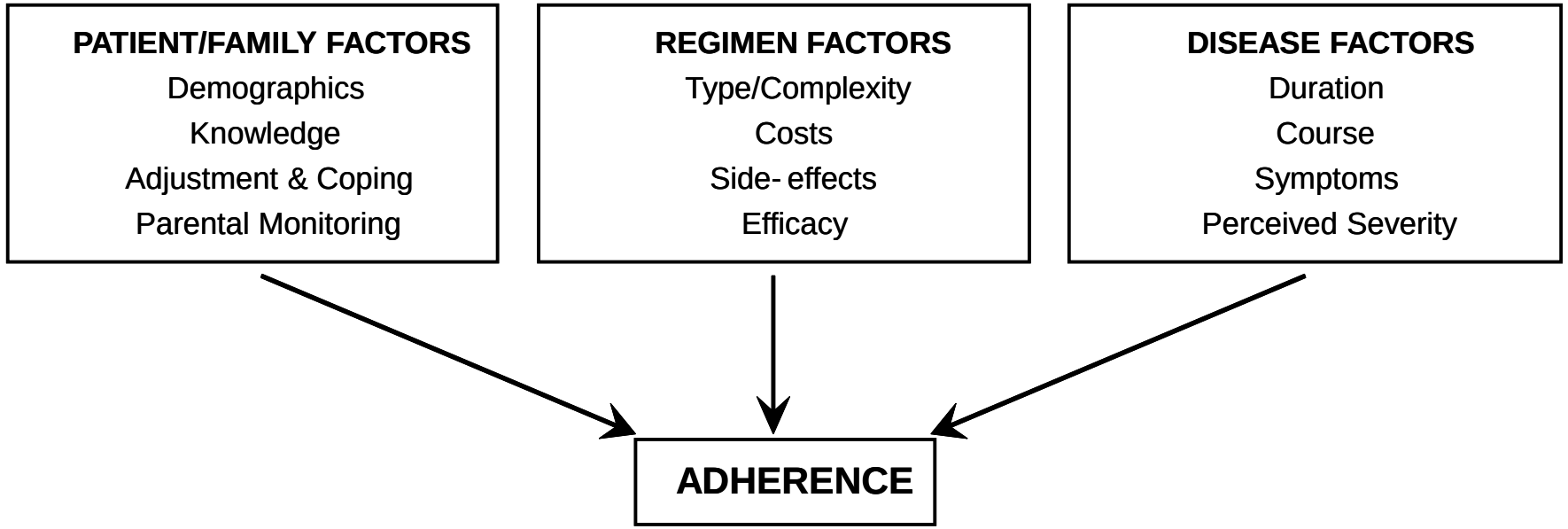
Paediatric obesity continues to be one of the most important health issues facing children and families today, and there remains a need for effective treatment options. There are a few reports in the literature demonstrating high rates of attrition from paediatric weight management programmes, ranging from 27% to 73%. While some studies show that racial/ethnic minorities, the economically disadvantaged and those with higher levels of obesity are at risk, other studies do not. There is some consistency in reasons given by families for attrition from treatment, most often scheduling issues and programmes not meeting family needs or expectations. This review highlights identified contributors to attrition from paediatric weight management and provides a framework to study this problem, based on models of adherence to paediatric medical regimens.

Background

- Summary: predictors of attrition*
  - Higher BMI/z-score
  - African-American race/ethnicity
  - Older age
  - Poorer health
  - Behavioral issues
- Why attrition matters
  - Wasted time, effort, and money
  - No outcome
  - “Failed” attempt: frustration, discouragement, learned helplessness

*Skelton Obesity Reviews 2011

Model of adherence to pediatric medical regimens



*Adapted from Rapoff

Predicting drop-out

If you could predict who might drop out of treatment, can you act to prevent it?

- Stay In Treatment (SIT) Study (originally titled “War of Attrition”), NIH R01 NR017639
- First multi-center study of attrition from pediatric weight management
  - Brenner Children’s Hospital
  - Boston Children’s Hospital
  - Children’s Mercy Hospital (Kansas City, MO)
  - Nationwide Children’s Hospital (Columbus, OH)

Outcomes Forecasting System

- Prediction modeling: using conventional approaches to find associations with outcome of interest (logistic regression)
- Usually site-specific: prohibits using larger, multi-site data sets that account for different predictor variables between sites

Table 2: Program participant characteristics

Predictors	Kansas	WFU	p
	N = 700	N = 1277	
Age (yrs)	11.1 (3.43)	11.7 (3.22)	<0.001
BMIz	2.4 (0.4)	2.5 (0.5)	<0.001
Race			0.003
Asian	9 (1.3%)	3 (0.2%)	
Black	179 (25.6%)	372 (29.1%)	
Hispanic	221 (31.6%)	327 (25.6%)	
Multiracial	29 (4.1%)	53 (4.2%)	
White	248 (35.4%)	500 (39.2%)	
Other	14 (2.0%)	22 (1.7%)	
Sex			0.121
Female	368 (52.6%)	728 (57.0%)	
Male	332 (47.4%)	548 (42.9%)	
Insurance			0.017
Commercial	210 (30.0%)	464 (36.3%)	
Government	461 (65.9%)	761 (59.6%)	
None/Other	29 (4.1%)	52 (4.1%)	
Drop-out	443 (63.3%)	734 (57.5%)	0.014

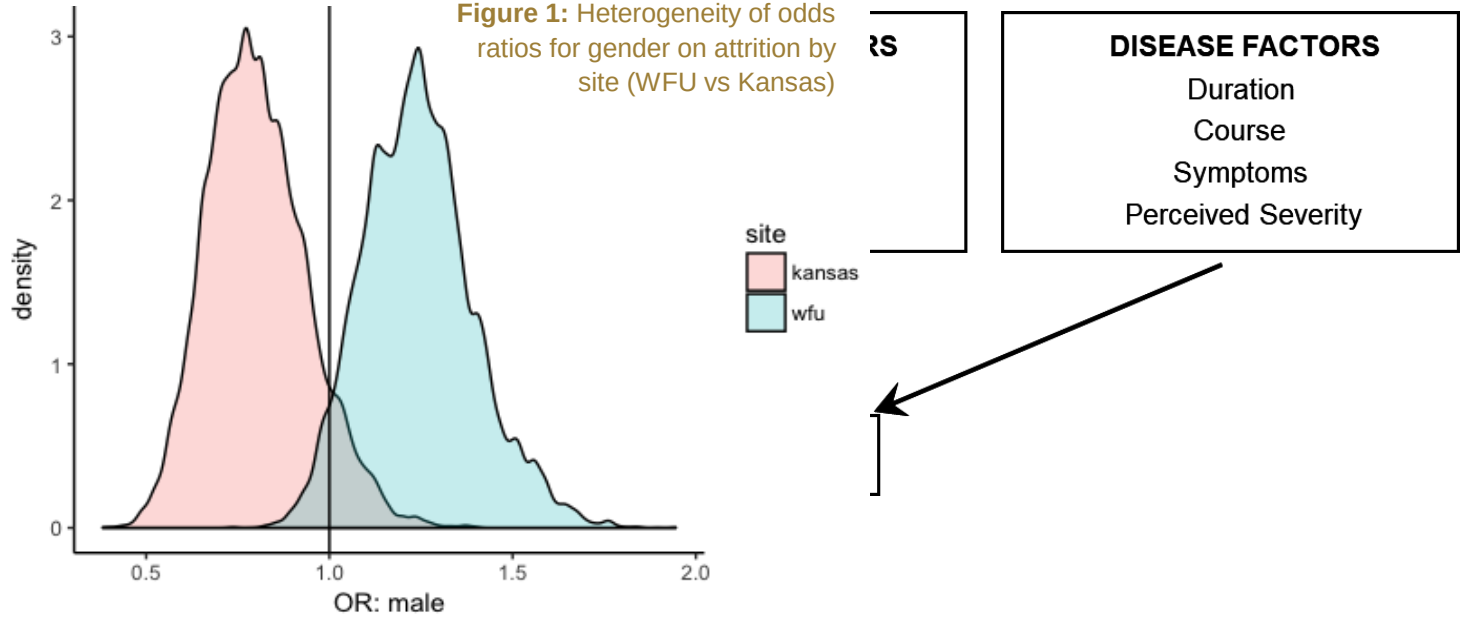
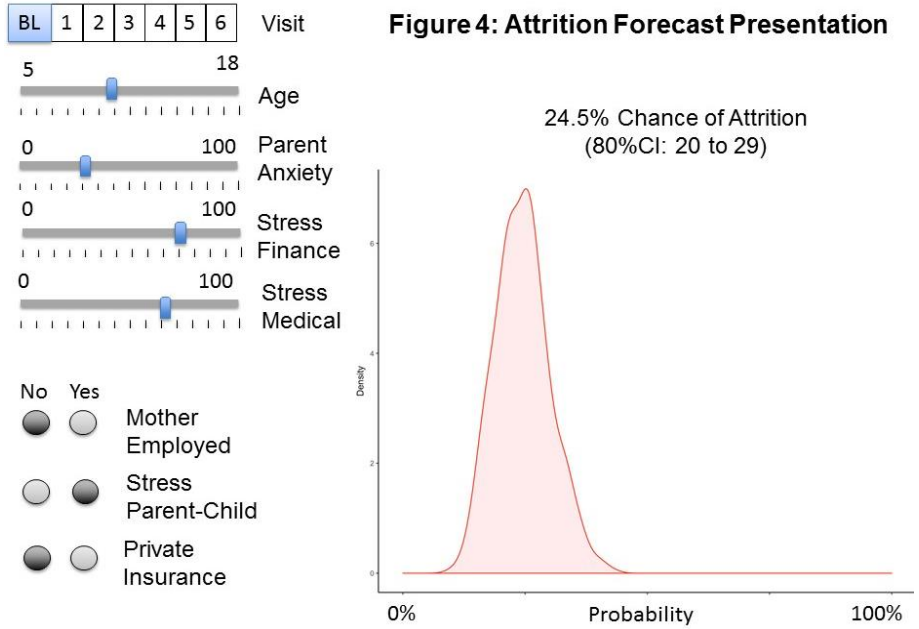


Figure 1: Heterogeneity of odds ratios for gender on attrition by site (WFU vs Kansas)

Outcomes Forecasting System

- Idea: use analytical approaches that can account for different sites with potentially different predictors of attrition by using prior probabilities
- Can be calibrated over time: more data, more precision
- Approaches:
  - Bayesian modeling: uses “best guesses” of odds ratios
  - Random Forest: uses output of multiple decision trees to predict



Outcomes Forecasting System

- Update: data collected on 400+ families (parent/child dyads) across 4 different pediatric weight programs
- Will be temporally and externally validated
- Pilot started to utilize in clinical settings:
  - Identify families at highest risk for dropout
  - Utilize evidence-based methods for retention
- Retention:
  - Establish relationships quickly: follow-up phone call
  - Personalized phone calls and texts
  - Monitoring of families at highest risk
  - Immediate contact if missed appointment

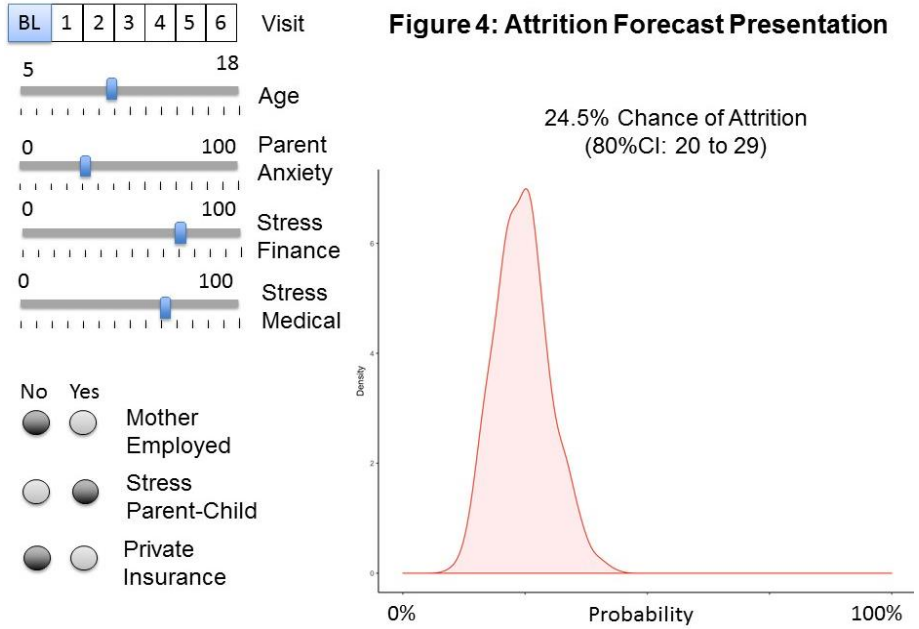


Figure 4: Attrition Forecast Presentation

A prediction model method for optimizing appointment overbooking in healthcare clinics using EHR data

NATHANIEL S. O'CONNELL, PHD

ASSISTANT PROFESSOR

BIOSTATISTICS AND DATA SCIENCE

“No-Shows” or Missed Appointments

- ‘No-show’: patient does not show up to their scheduled clinic visit or appointment
- An average of 23% of outpatient clinic visits scheduled result in ‘no-shows’, with rates ranging from 5-55%
- “No shows” lead to loss of revenue and productivity in clinics and unnecessarily prevent/delay access to care for others in need.

Scheduling and Overbooking Practices

- Predictive Overbooking: overbooking patients predicted as high risk of being a ‘no-show’ with additional patients during the same time-slot [1-5]
- A lot of attention has been given to optimizing *scheduling* to account for patient no-shows [2-5]
  - Assume good prediction model exists
  - Difficult to implement
- Less attention given to optimizing a *prediction model itself* in the context of being used for predictive overbooking.

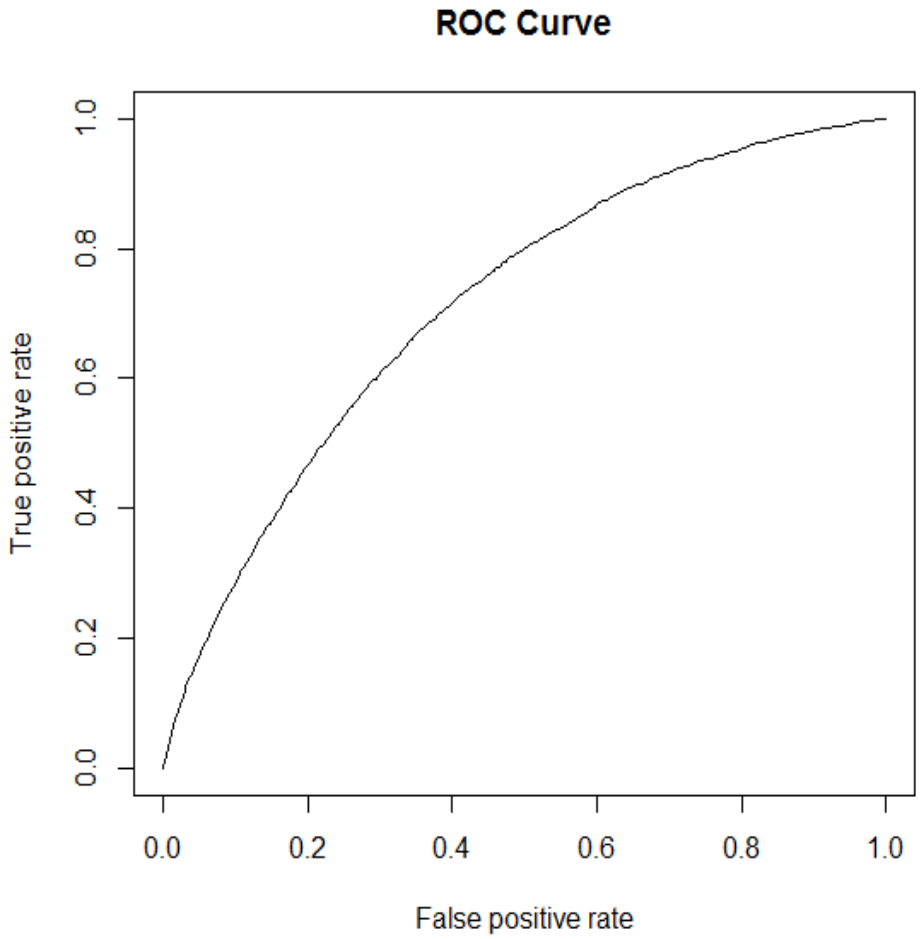
Evaluation in terms of Overbooking Model…

- Clinic Capacity = number of available appointment slots in a day
- Clinic Utilization = number of patients who ‘show’ in a day
- Costs are dynamic. As clinic utilization increases, relative costs of no-shows decrease while cost of double-shows increase.
  - Implication: we want to double-book just enough patients so that the expected number of patients to show up in a day equals the number of appointment slots available.

Clinical efficiency is maximized when clinic utilization equals clinic capacity

Real world EHR Data Application

- 126,189 scheduled pediatric patient visits across 13 pediatric subspecialty clinics from 2013-2018 at Brenner Children's Hospital
- Random Forest prediction model for each subspecialty clinic
  - Training data=70%; validation data = 30%; 250 trees for
  - Mean AUC across models = 0.713
- Top 5 predictors included:
  - Pediatric Medical complexity
  - Lead Days
  - Insurance
  - Prior No shows
  - Prior shows



Validation Set Results

Average Estimated Cost to a Clinic on a Given Day

	No Overbooking	Proposed Approach	Youden Index	>0.5
Cardiology	$126.93	$26.25	$291.76	$408.54
Clinical Nutrition	$255.10	$61.79	$148.73	$148.73
Developmental	$184.93	$65.57	$116.99	$323.80
Endocrinology	$161.41	$34.00	$102.24	$280.37
Gastroenterology	$191.49	$26.64	$213.37	$230.92
Genetics	$156.68	$24.33	$280.31	$300.16
Infectiouse Disease	$197.21	$84.63	$320.17	$306.32
Nephrology	$137.51	$26.03	$244.10	$308.83
Otolaryngology	$160.92	$62.48	$294.75	$447.81
Psychology	$87.61	$63.89	$156.15	$620.94
Pulmonary	$152.39	$34.33	$475.29	$334.27
Rheuomatology	$153.63	$35.06	$445.76	$337.15
Speech-language	$169.25	$37.03	$156.83	$221.21

Estimated Clinic Utilization per day (Capacity = 18)

	No Overbooking	Proposed Approach	Youden Index	>0.5
Cardiology	15.46	17.8	21.3	22.69
Clinical Nutrition	12.9	18.39	19.46	19.46
Developmental	14.3	18.49	19.13	21.6
Endocrinology	14.77	17.71	18.98	21.12
Gastroenterology	14.17	17.95	20.29	20.51
Genetics	14.87	17.97	21.12	19.8
Infectiouse Disease	14.06	18.71	21.58	21.41
Nephrology	15.25	17.85	20.7	21.48
Otolaryngology	14.78	18.49	21.29	23.13
Psychology	16.25	16.82	19.7	25.23
Pulmonary	14.95	18.18	23.48	21.78
Rheuomatology	14.93	18.17	23.11	21.8
Speech-language	14.62	18.19	19.63	20.41

Cost of patient wait time = $10 for each double booked patient

Cost of clinic idle time = $50 for each missed appointment while clinic utilization $<$ clinic capacity

Cost of clinic = $75 for each patient when clinic utilization $>$ clinic capacity

Conclusions

- Our proposed optimization approach is easy to implement into prediction models
- Our approach maximizes clinical efficiency, leading to cost-savings for a clinic
- Continuing work:
  - Obtain larger data sets to build stronger models
  - Extending our approach to account for the variability around estimated clinic utilization to further improve the model.
  - Incorporate the approach in to more complex ‘predicative overbooking’ scheduling algorithms for further improvements
  - Pilot test: implementing model into Epic, and testing in clinical settings

High-Dose Methotrexate Containing Induction Chemotherapy Followed by Nivolumab Consolidation in Older (≥ 65) Patients with Previously Untreated Primary CNS Lymphoma (LCI-HEM-PCNSL-001)

Steven I Park[1], Lakshmi Nayak[2], Danielle Boselli[3], Raphael E Steiner[4], Ashley L Sumrall[5], Nazanin K Majd[6], Xhevahire Begic[7], Sarah Norek[7], Christopher Dittus[8]

[1]Department of Hematologic Oncology and Blood Disorders, Levine Cancer Institute, Wake Forest University, Atrium Health, Charlotte, NC
[2]Center for Neuro-Oncology, Dana-Farber Cancer Institute, Brigham and Women's Hospital, Harvard Medical School, Boston, MA
[3]Department of Cancer Biostatistics, Levine Cancer Institute, Atrium Health, Charlotte, NC
[4]Department of Lymphoma & Myeloma, University of Texas MD Anderson Cancer Center, Houston, TX
[5]Department of Solid Tumor Oncology, Levine Cancer Institute, Atrium Health, Charlotte, NC
[6]Department of Neuro-Oncology, University of Texas MD Anderson Cancer Center, Houston, TX
[7]Sponsored Research Coordinating Center, Levine Cancer Institute, Atrium Health, Charlotte, NC
[8]Division of Hematology, University of North Carolina, Chapel Hill, NC

Atrium Health

Wake Forest University School of Medicine

Background

- PCNSL is an aggressive subtype of non-Hodgkin lymphoma involving CNS organs, including the brain parenchyma, leptomeninges, and spinal cord

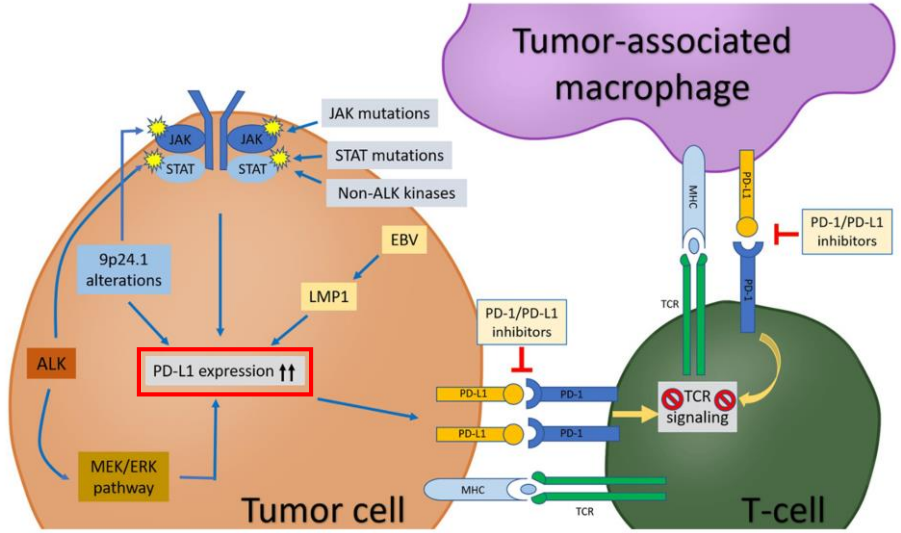
- Current standard for primary CNS lymphoma (PCNSL): High-dose methotrexate (HD-MTX)-containing chemotherapy followed by either autologous stem cell transplant (ASCT) or whole-brain irradiation (WBI)

- Older frail patients with PCNSL are unable to undergo ASCT or WBI due to increased risk of treatment-related toxicity

- Without consolidation, survival outcomes are significantly worse, with a 3-year progression free survival (PFS) rate of ~ 30%. Therefore, novel therapeutic approaches are needed for older PCNSL patients

Background

- Nivolumab, an anti-PD1 antibody, has shown promising clinical activities in PCNSL (9p24.1 amplification with PD-L1/L2 overexpression)
- In a small study of relapsed/refractory PCNSL, nivolumab was associated with high response rates (n = 5, 100% ORR with 4 CR/nCRs and 1 PR). 3 out of 5 achieved sustained remission (Nayak L et al. Blood 2017)
- Our study evaluated nivolumab as consolidation in the frontline setting for PCNSL in older (≥ 65 years) patients who are deemed poor candidates for WBI or ASCT
- We hypothesize that addition of nivolumab in the frontline setting will be safe and improve survival outcomes of older PCNS patients without toxicities associated with WBI or ASCT



Biomedicines 2022;10:1507

Atrium Health

Wake Forest University School of Medicine

Objectives

Primary Objective:

- Stage 1: To evaluate the safety of nivolumab consolidation after completion of HD-MTX containing induction chemotherapy in terms of a tolerated dose (based on DLTs) for the expansion phase (Stage 2)

- Stage 2: To evaluate the efficacy of nivolumab consolidation after completion of HD-MTX containing induction chemotherapy in terms of the 2-year PFS rate and compare to relevant historical controls.

Objectives

Secondary and Exploratory:

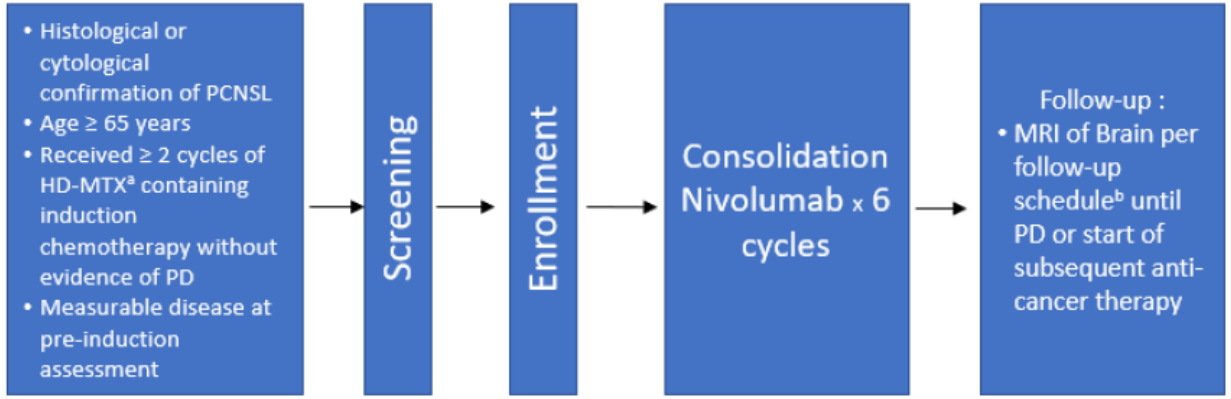
- To evaluate the safety and toxicity profile of nivolumab
- To evaluate progression-free survival (PFS)
- To evaluate overall survival (OS) and estimate the OS rate at 2 years
- To describe change in response from completion of HD-MTX containing induction chemotherapy, prior to initiation of nivolumab consolidation therapy, to the end of nivolumab consolidation therapy
- To perform RNA-seq and assess 9p24.1 copy number alteration to correlate with treatment response

Study Design

This is a single-arm, two-stage, Phase 1B study to evaluate the safety (Stage 1) and efficacy (Stage 2) of nivolumab in PCNSL

<u>Two-Stage Design</u>:

- **Stage 1 (3+3)**: up to 6 subjects at 480 mg nivolumab Q 28 days
  - ➢ If < 2 out of 6 subjects experience DLT, will continue enrolling into Stage 2
- **Stage 2**: up to 14 additional subjects at 480 mg nivolumab Q 28 days
  - ➢ Total of up to 20 evaluable subjects



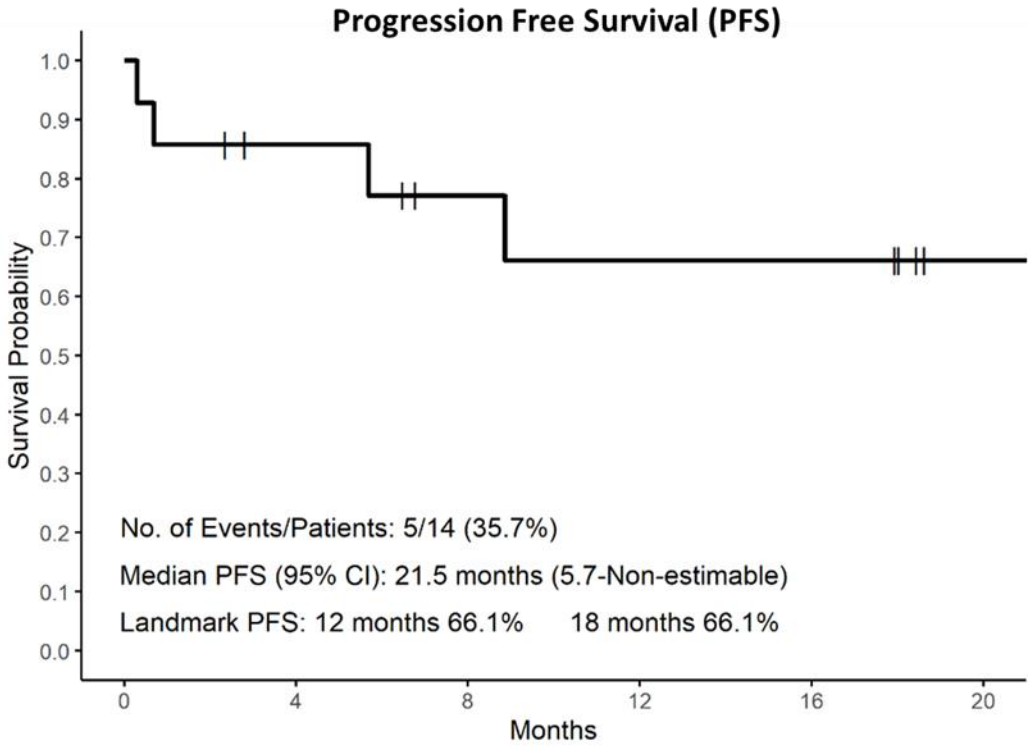
[a] HD-MTX= high-dose methotrexate
[b] MRI Brain 8 weeks after last dose of nivolumab (± 2 weeks) then every 4 months (± 2 weeks) x 1 year, every 6 months (± 2 weeks) x 1 year; then at the frequency as determined by the investigator

Key Inclusion Criteria

- Histological or cytological confirmation of **PCNSL**, CD20 positive by immunohistochemistry
- Age **≥ 65 years** at time of informed consent
- Measurable disease **at the time of diagnosis** (i.e. prior to pre-study HD-MTX induction) including lesions that can be accurately measured in 2 dimensions by MRI of brain and have a greatest transverse diameter of 1 cm or greater. MRI of brain (and spine if indicated) must have been obtained prior to initiation of pre-study HD-MTX induction
- Eastern Cooperative Oncology Group (ECOG) **performance status of 0-3** within 14 days prior to D1 of study treatment
- Deemed **poor candidate for whole brain irradiation (WBI) and/or autologous stem cell transplant (ASCT)** due to poor functional status (ECOG 2 or 3) or advanced age (≥ 65), or in the opinion of the treating physician, subject would not tolerate the consolidative WBI and/or ASCT for other reasons
- Females of childbearing potential (FCBP) must have a **negative serum pregnancy test** within 3 days prior to D1 of treatment

Preliminary Results

Characteristic	Total (N = 14)
Age, median [range]	71.5 [65, 79]
Gender, N (%)	
Female	10 (71.4)
Male	4 (28.6)
Race, N (%)	
Black	1 (7.1)
White	13 (92.9)
Ethnicity, N (%)	
Hispanic or Latino	3 (21.4)
Non-Hispanic or Latino	11 (78.6)
ECOG at enrollment, N (%)	
0	5 (35.7)
1	4 (28.6)
2	4 (28.6)
3	1 (7.1)
Induction regimen, N (%)	
RMPV (rituximab, methotrexate, procarbazine, vincristine)	5 (35.7)
MATRix (methotrexate, cytarabine, thiotepa, rituximab)	1 (7.1)
Other; Methotrexate, rituximab	1 (7.1)
Other; Methotrexate, rituximab, temozolomide	3 (21.4)
Other; High-dose methotrexate, rituximab	2 (14.3)
Other; Dose-reduced high-dose methotrexate, rituximab, temozolomide, cytarabine	1 (7.1)
Other; DeAngelis	1 (7.1)
Time to nivo start from induction end (Months), median [range]	1.2 [0.6, 4.3]



Atrium Health

Wake Forest University School of Medicine

Participating Sites and Funding Sponsor

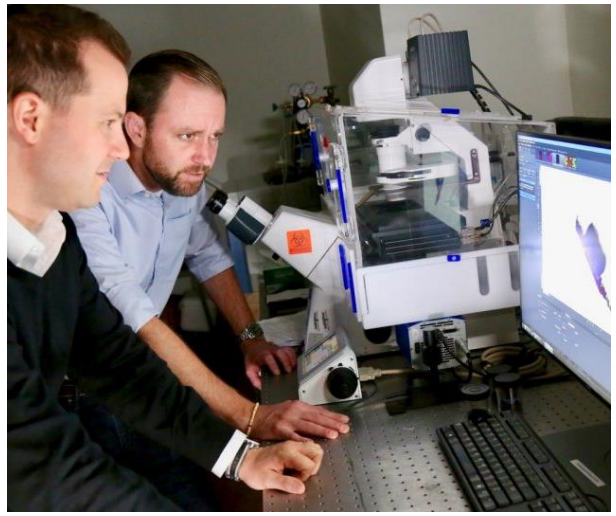
- Participating Sites:
  - Levine Cancer Institute, Wake Forest Baptist, Atrium Health, Charlotte, NC - Coordinating Center
  - Dana-Farber Cancer Institute, Harvard, Boston, MA
  - UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC
  - University of Texas MD Anderson Cancer Center, Houston, TX

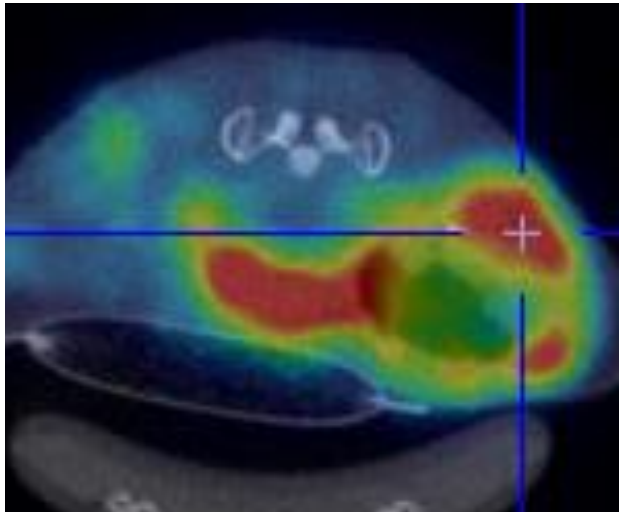
- Funding Sponsor: Bristol-Myers Squibb (BMS)

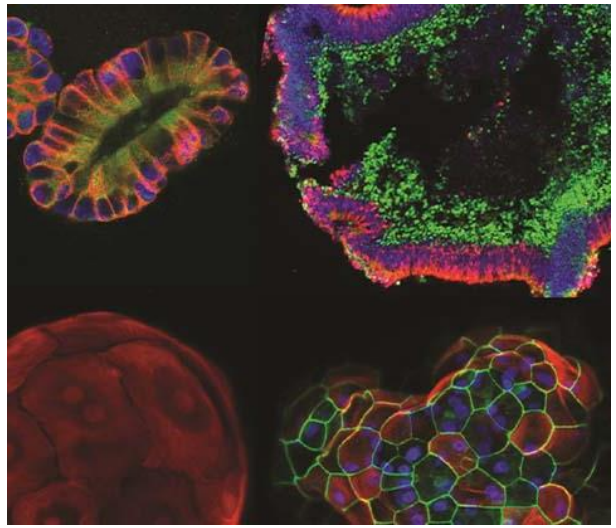
Sponsor Contact Information

Name	Role	Contact
Steven Park	Sponsor-Investigator • Serves in both sponsor and site roles	704-403-1322 steven.park@atriumhealth.org
Sarah Norek	Clinical Project Manager • Clinical/enrollment oversight • Protocol clarifications • Cohort management	803-370-8652 sarah.norek@atriumhealth.org
Carrie Syfert	Clinical Project Coordinator • SAE/deviation reporting	704-451-5326 carrie.syfert@atriumhealth.org
Jackie Begic	Data Project Manager • eCRF questions • OnCore calendar questions	980-442-2306 xhevahire.begic@atriumhealth.org
Elise Tjaden	Data Project Coordinator • eCRF questions • OnCore calendar questions	716-553-7570 elise.Tjaden@atriumhealth.org
Tamela Kyryliuk	QA Monitor	980-442-2366 tamela.kyryliuk@atriumhealth.org
Chasity Kinder	Regulatory Coordinator	704-747-8793 chasity.kinder@atriumhealth.org

Questions?







Panel Discussion

SCALABILITY

AND

HEALTH EQUITY

Networking LUNCH

BIOTECH PLACE ATRIUM

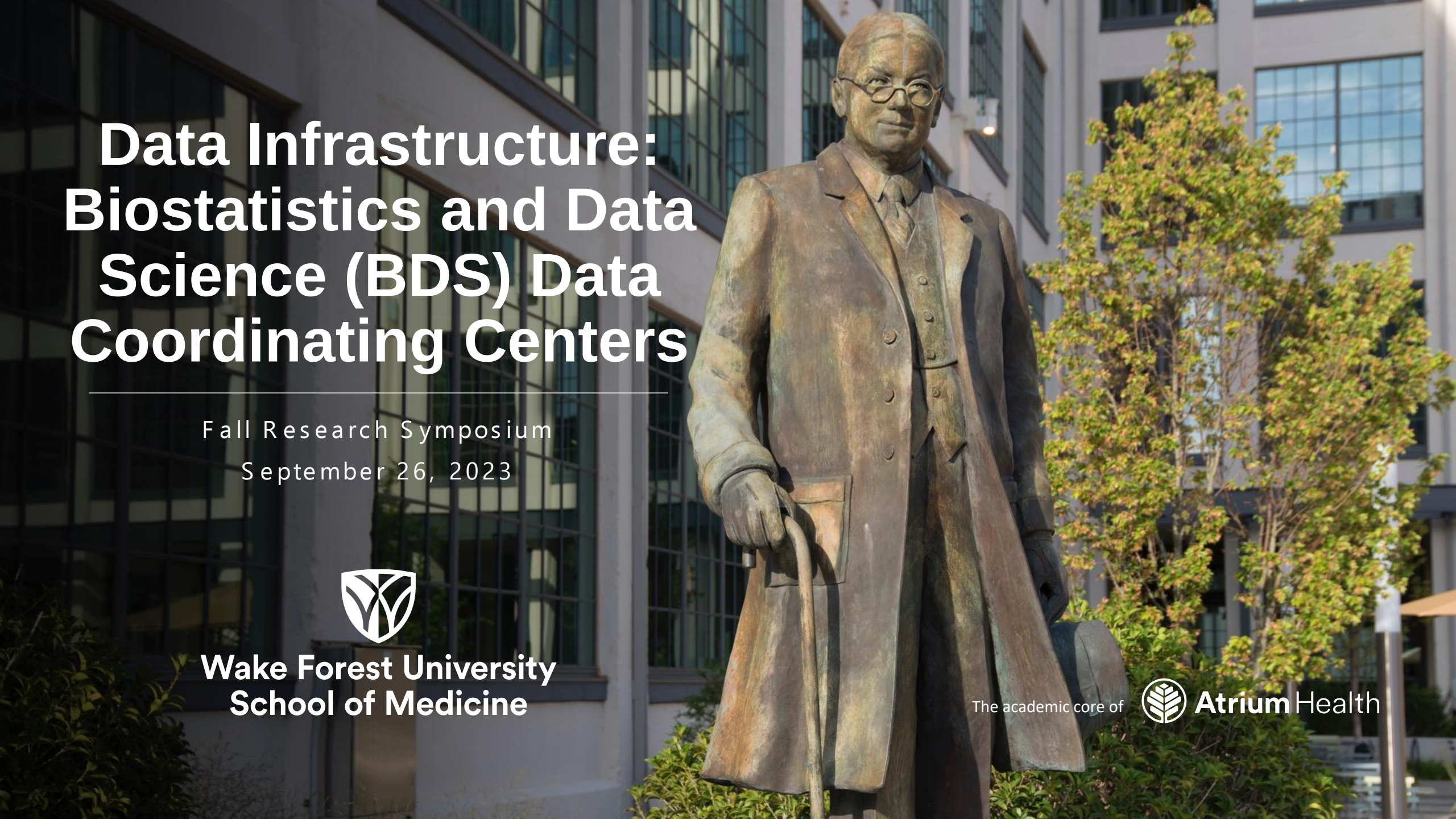
Clinical Trial Resource Offerings

EMILY DRESSLER, PHD

JENNIFER REEVES, MHA, RN, BSN

GOLDIE SMITH BYRD, PHD

JOHN SANDERS, MS, MPH



Data Infrastructure: Biostatistics and Data Science (BDS) Data Coordinating Centers

Fall Research Symposium

September 26, 2023

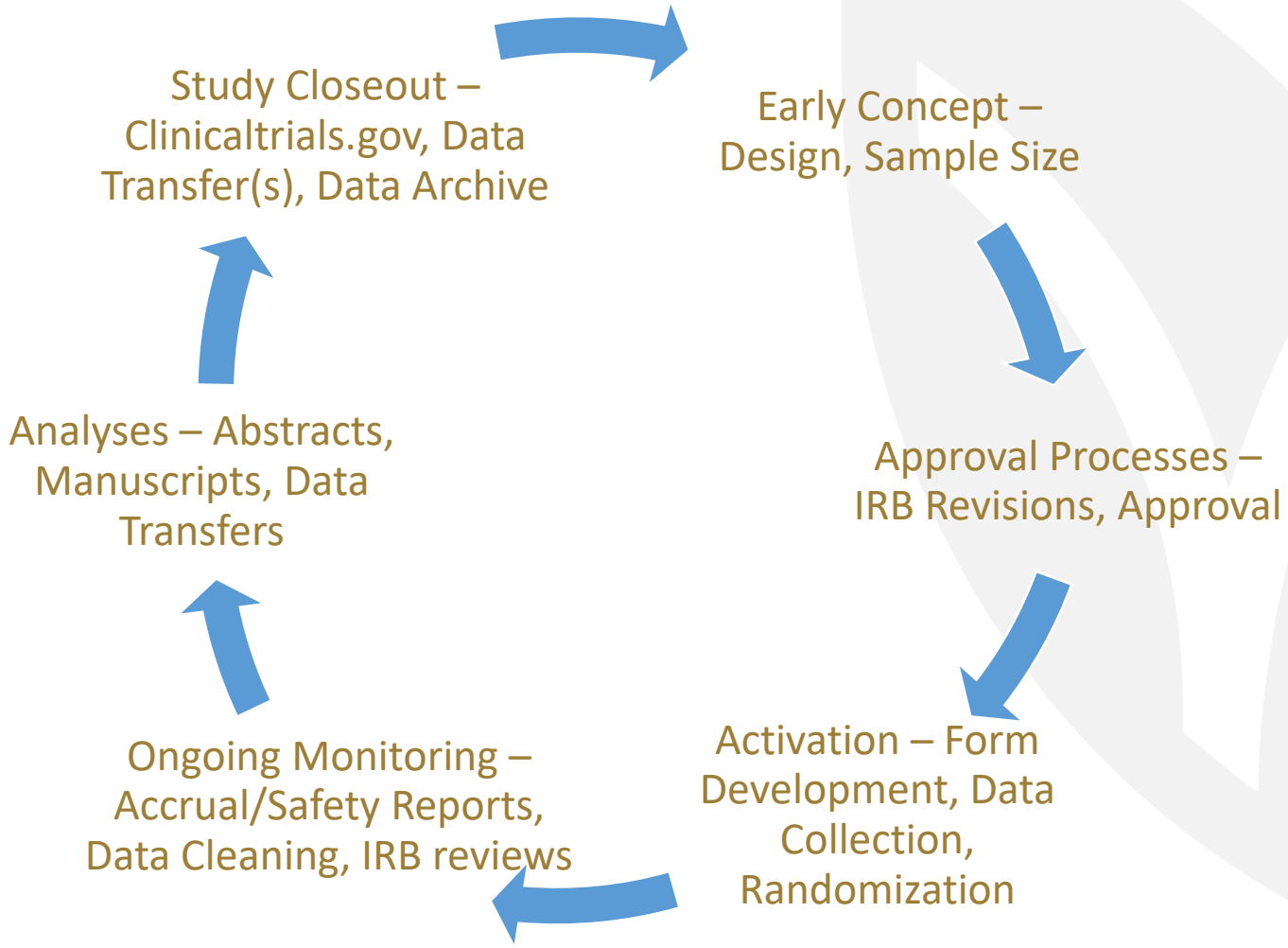
Wake Forest University
School of Medicine

The academic core of Atrium Health

What is a Data Coordinating Center (DCC)?

- DCCs coordinate all things data and study design!
- WFUSM Department of Biostatistics and Data Science (BDS) within the Division of Public Health Sciences (PHS) has vast experience with coordination of multi-center trials
  - 30+ years of trial experience
  - Pioneered some of the first web-based entry systems for trial data collection and management
  - Extensive funding and collaboration with NIH, NHLBI, NCI, among others
- We view clinical trial conduct and coordination as a scientific undertaking

Statistical input throughout study lifespan



BDS Brief DCC History

- **Trials**
  - ACCORD (1995-2015) N=10,251
    First web-based trial!
  - Look AHEAD (1999-2020) N=5,145
  - SPRINT (2009-2019) N=9,361
  - LIFE (2009-2015) N=1,635
  - MoTrPAC (2016-2025) N=varies
  - US POINTER (2017-2030) N=2,000
  - PREVENTABLE (2019-2026) N=20,000
  - Lots of NCORP studies
  - Many smaller studies

- **Observational Studies**
  - IRAS (1992-1999) N=1,625
  - IRAS Fam (1999-2009) N=1,861
  - SEARCH (2000-2021) N=7,400
  - HEIRS (2000-2007) N=101,168
  - T1DGC (2002-2011) N=14,903
  - GUARDIAN (2010-2015) N=4,685
    DNA samples
  - APOLLO (2017-2023) N=2,614

DCC People

- Faculty Biostatisticians
  - Oversee all components of DCC, Responsible for study design, sample size, analytic plan
- Project Managers
  - Protocol development, set priorities and tasks
  - Collaborate with clinical coordinating center (CCC) project managers
  - Coordinate with site staff, answer questions
- Programmers
  - Data Website and Data Entry Systems
  - Form Development, Branching logic, Security
- Staff Biostatisticians
  - Dynamic live reports, Analyses, Presentations, DSMB reports
- Data Managers
  - Monitor data entry, quality control, query for missing or incorrect data
  - Represent DCC on study meetings

Data platforms

- DEACON is our template data management platform
  - Developed and refined over 30+ years and many DCCs
  - Integrates data collection, study operations/management, and reporting/QC
  - Allows for the development of custom workflows and tools
  - Really is more trial management than just EDC
- Also have extensive experience running trials and studies in REDCap

How to collaborate with us?

- We are not exactly a resource right now…
  - Requires grant funding to establish a DCC with the necessary resources to run it effectively
  - Expectation of faculty biostatisticians as MPI of main project or PI of DCC (if separate grant)
- We are definitely available to CLT researchers too!
- If interested, please contact:
  - BDS chair: Walter Ambrosius (walter.t.ambrosius@wakehealth.edu) and/or
  - Vice Chair: Emily Dressler (emily.dressler@wakehealth.edu)

- Non-grant funded studies can still utilize CTSI resources for study setup, BERD biostatisticians, etc.
- Plans to integrate data coordination with Advocate Health National Center for Clinical Trials

Clinical Research Unit

Winston Salem market

Coming soon to Charlotte market

Atrium Health

Wake Forest University
School of Medicine

Clinical Research Unit

Located on the first floor of the Sticht Center

Wake Forest Baptist Medical Center

- Provides space, bionutrition, laboratory, and patient care services for approved studies
- Team works closely with investigators and their study teams to provide high-quality services for all types of studies including industry, federal, and investigator initiated sponsored research
- Available services include:
  - Clinical research space
  - Patient care services
  - Laboratory processing and specimen management
  - Bionutrition services

Patient care services - Nursing

Examples of patient care services the CRU can provide include:

- Vital signs and height/weight measurements
- Study-related infusions
- Phlebotomy services, including PK studies and clotting time procedures
- Assistance with lumbar punctures, biopsies, bronchoscopies, and other minor procedures
- Study medication administration
- 12-lead EKGs and cardiac monitoring
- Continuous blood pressure monitoring
- Conscious sedation
- Eye chart and hearing testing
- Oral glucose tolerance testing (OGTT)
- Mental and cognitive testing
- Metered walk and physical testing

Patient care services - Laboratory

Examples of services the CRU lab can provide include:

- Study-related processing of blood, saliva, sputum, urine, CSF, and fecal specimens
- Isolation of specific cells (PBMCs, RNA, T-cells)
- IV and oral glucose tolerance testing
- Pharmacokinetic (PK) and Pharmacodynamic (PD) specimen processing
- Preparation and routing of specimens for immediate analysis
- Preservation and shipment of specimens for transport of ambient, refrigerated, and frozen specimens
- Short-term and long-term storage of specimens
- Storage and shipment of pre-cut tissue samples
- Waive testing (HemoPoint and urine pregnancy)
- Non-waived testing (YSI 2300 STAT Plus Glucose Analyzer)
- CAP and COLA-certified moderate-complexity lab

Patient care services - Bionutrition

Examples of bionutrition services the CRU can provide include:

- Research diet development, analysis and preparation
- Recipe development
- On-site and pack out research diet feeding
- Computer-assisted food weigh-back system
- Healthy snacks for fasting visits
- Dietary compliance monitoring and assessment
- Nutritional status and dietary history assessments
- Nutrition screening and evaluation for feeding study eligibility
- Anthropometric and bioelectrical impedance measurement
- Indirect calorimetry testing
- Nutrition education and counseling by Registered Dieticians
- Development of protocol-specific educational materials

Accessing CRU services

- Indicate CRU need on eIRB application
- CRU team will schedule an initial meeting to review study needs and CRU services requested
- CRU guidelines will be developed and reviewed with study team; PI will sign prior to study activation and participant scheduling in CRU
- CRU scheduling turnaround time is 24-48 hours; please plan accordingly
- Pricing information available here (2024 pricing to come soon):

  document-3cru-services-pricing-grid-2023-final-121222.pdf (atriumhealth.org)
- More information about the CRU and a virtual tour can be found here:

  Clinical Research Unit | Research Administration / CTSI (wakehealth.edu)

Charlotte Clinical Research Unit

- Target opening mid-2025
- Initial location will be 1043 E. Morehead St. (South State Bank building)
- Permanent location will be in The Pearl (5-7 years)
- Initial unit will be smaller than current Winston Salem unit
- Faculty and Investigators surveyed to help determine services that will be offered in Charlotte market initially
- More to come!

Integrating Special Populations (ISP)

Goal: Increase volume and impact of research that relates to special populations

Aim1: Serve as an institutional hub for outreach and engagement of special populations

Aim 2: Facilitate enrollment and retention of special populations in clinical research

Aim 3: Increase research that includes special populations by building capacity and engendering trust and respect through education and skills development

Special Populations include a wide range of individuals:

- Older adults and children
- Underrepresented racial and ethnic groups
- Underrepresented sex and gender groups
- Males
- Rural and under-resourced communities and residents
- Other groups not well-represented in research

Our ISP TEAM

Goldie Byrd, PhD
Director

Capri Foy, PhD
Associate Director

Allison Caban-Holt, PhD
MACHE Consultant

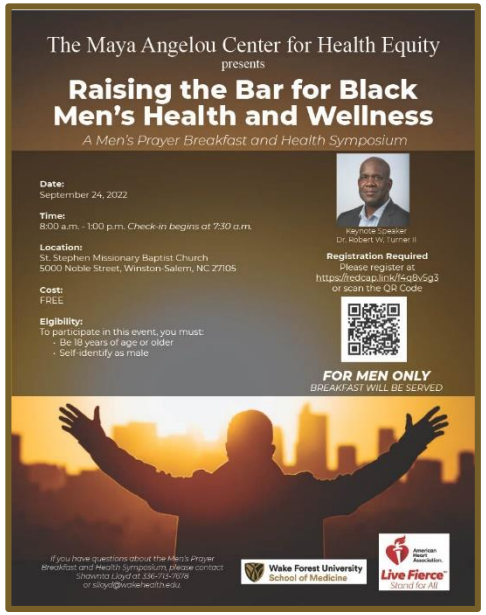
Kimberly Montez, MD
Pediatrics Faculty

Temana Aguilar, PhD
Administrative Director

Laura McDuffie, MS
Research Associate

ISP Outreach and Engagement Connect Communities to the Clinical and Research Communities

We assure *sustained presence* in diverse communities to build trust *and trustworthiness*:



Conferences

Workshops

Cultural Ceremonies

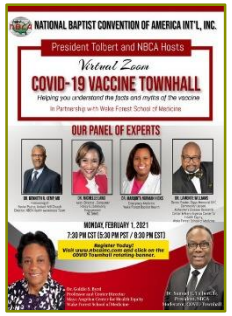
Charity Walks and Health Ambassador Trainings

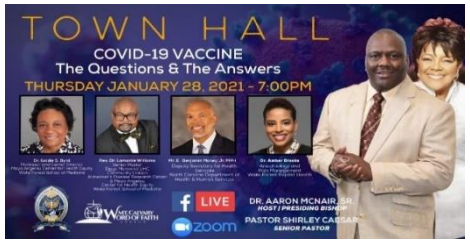
Wake Forest University School of Medicine

MAYA ANGELOU CENTER FOR HEALTH EQUITY and Integrating Special Populations

Leaders Leading Leaders

MACHE and TPN Town Halls and Webinars on **COVID-19 Awareness and Education**
Reached Over 400,000 African Americans in 2021 - 2022





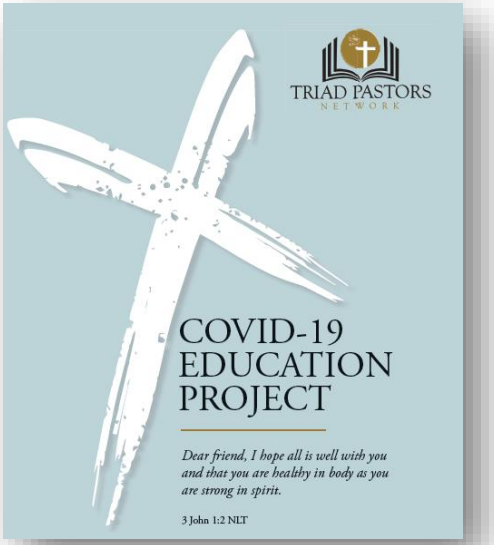
LEADERS LEADING LEADERS
12 Town Halls
Reached over 400,000

ISP Facilitates Enrollment of Special Populations

	FY 2022	FY 2023	FY 2024 As of 09/22/2023
Language Services	19	10	2
Consultations	2	2	0
Research Participant Navigation	1	3	0
Other	4	3	0
Total	**26**	**18**	**2**
Voucher Applications	6	8	0

ISP Facilitates Research with Special Populations

- We design research with community
- We implement projects with community
- We publish with community
- We return results to community



COVID-19 Education Results Booklet Returned to Community

EXAMPLES:

Foy CG, Lloyd SL, Williams KL, Gwathmey TM, Caban-Holt A, Starks TD, Fortune DR, Ingram LR, Byrd GS. Gender, Age and COVID-19 Vaccination Status in African American Adult Faith-Based Congregants in the Southeastern United States. J Racial Ethn Health Disparities. 2023 Aug 14. doi: 10.1007/s40615-023-01744-w. Epub ahead of print. PMID: 37580437.

Lloyd SL, ***Foy CG,*** Caban-Holt A, Gwathmey T, Williams KL, Starks TD, Mathews A, Vines AI, Richmond A, Byrd GS. Assessing the Role of Trust in Public Health Agencies and COVID-19 Vaccination Status Among a Community Sample of African Americans in North Carolina. J Racial Ethn Health Disparities. 2023 Jun 5:1–11. doi: 10.1007/s40615-023-01646-x. Epub ahead of print. PMID: 37273163; PMCID: PMC10241131.

Martinez LS, Brinkerhoff CA, Howard R, Feldman J, Kobetz J, White T, Berhalter LT, Bilheimer A, Hoffman M, Isasi CR, Killough C, Martinez J, Chesley J, Baig AA, ***Foy C***, Islam N, Petruse A, Rosales C, Kipke M, Baezconde-Garbanati L, Schroder R, Battaglia TA, Lobb R. Strategies to promote language inclusion at 17 CTSA Hubs. Journal of Clinical and Translational Science

Available to CLT Researchers

- ISP is available to CLT researchers.

- If interested, please contact:
  - Capri Foy (cfoy@wakehealth.edu)
  - Goldie S. Byrd (gbyrd@wakehealth.edu) or

- QR Code to ISP Website:

RESEARCH REIMAGINED

JAVARA EMBEDS research staff and infrastructure into healthcare organizations to provide patients' clinical research access through their trusted physician

HEALTHCARE PARTNERS

PROVIDES:

- Access to identified, diverse patient populations
- Patients clinical research access through their trusted physician

+

JAVARA

PROVIDES centralized resources and standardized operations including:

- Regulatory and QA Support
- Feasibility Support
- Contract & budget negotiations
- Clinical Research Coordinator Staff

RESULTS:

Accelerating research through innovation.

- Higher enrollment & retention
- Consistent quality & delivery
- Faster study start-up, timely data
- Quality outcomes

AHWFB/Javara PARTNERSHIP History

PURPOSE: Build culture & framework to achieve expansion and scale of research participation

2022

- Partnership spanning 6 departments
- Multi-specialty portfolio of trials active & awarded
- Engaged in Racial Equity Task Force – focus on diversity in research

2020

- Partnership spanning 2 departments
- Investigator initiated trial: $40M+ Including federal/state grant
- Virtual surveillance study of more than 20K+ participants
- Operation Warp Speed - Moderna

2018

- Learning health system commitment to enterprise reach for clinical research as a care option
- Partnership initiated in Department of Cardiology
- Advisory role to clinical research educational programs



AHWFB/Javara Current State

JAVARA

- Academic faculty departments working with Javara:
  - Infectious Disease
  - Epidemiology and Prevention
  - Endocrinology and Metabolism
  - Pediatric Hematology and Oncology
- Wake Health Network Specialties working with Javara
  - Ophthalmology
  - Family Practice
  - Pediatrics

Interested in learning how Javara might be able to support your research needs?

Contact Will Combs

phone: 336-464-7136

email: will.combs@javararesearch.com

BREAK

BIOTECH PLACE ATRIUM

Break Out Sessions

Break Out Session # 1

Biotech Auditorium

“Low Hanging Fruit”

Led By:

- **Kevin High, MD**
- **Kristie Foley, PhD**

Break Out Session # 2

Biotech Place Atrium

“Reaching the Brass Ring”

Led By:

- **Lynne Wagenknecht, DrPH**
- **Jamy Ard, MD**

Atrium Health

Wake Forest University School of Medicine

Closing Remarks

L. EBONY BOULWARE, MD, MPH