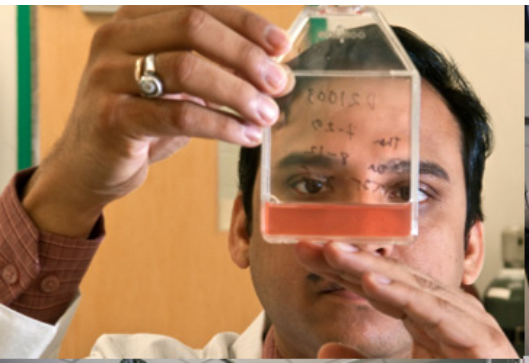
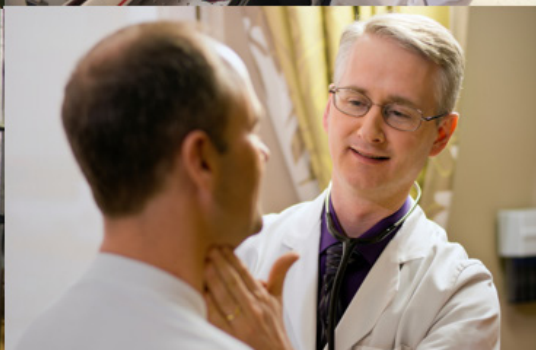
Department of Internal Medicine

Top Papers Published in 2020



Wake Forest® School of Medicine

Wake Forest® Baptist Health

Atrium Health

We are delighted to announce the Department of Internal Medicine's awards for the Top Research Papers published in 2020.

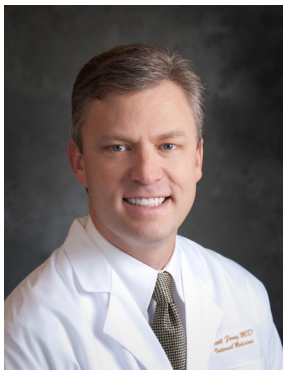
The 15 papers receiving recognition this year reflect the collective work of Internal Medicine faculty in Winston-Salem and Charlotte. The impact of bringing our two departments together as one provides a clear example that "We are better together."

The 15 papers were selected on the basis of their originality and their scientific and clinical impact. The papers span the spectrum of basic, clinical, and healthcare delivery science and represent the creativity, passion, and dedication of our faculty and trainees. The papers further demonstrate the Department's commitment to improve the health of the patients we serve by advancing understanding of the mechanisms of disease, by testing novel therapies, and by building and implementing the evidence base for clinical practice. Lastly, the papers represent the Department's long-term goal of advancing a preeminent Academic Learning Health System.

Please join us in congratulating this year's awardees. But recognize that the 15 papers receiving awards this year represent just the tip of the iceberg of the wonderful research being done by so many faculty and trainees in the Department.

Gary E. Rosenthal, MD, FACP
Tinsley R. Harrison
Professor and Chair
Department of
Internal Medicine

David M. Herrington, MD, MHS
Dalton McMichael Chair in
Cardiovascular Medicine
Vice Chair for Research
Department of Internal Medicine



Scott L. Furney, MD
Regional Chairman
Department of
Internal Medicine

Raghunatha Yammani, PhD

Age-Related Decline in Expression of Molecular Chaperones Induces Endoplasmic Reticulum Stress and Chondrocyte Apoptosis in Articular Cartilage

Citation: *Aging and Disease. 2020 Oct 1;11(5):1091-1102.*

Authors: Tan L, Register TC, Yammani RR

Summary: This study demonstrated that aging promotes loss of proteostasis and induces endoplasmic reticulum (ER) stress and chondrocyte apoptosis in articular cartilage. Thus, restoring proteostasis using a chemical/molecular chaperone or ER stress inhibitor could be a therapeutic option to treat aged-linked osteoarthritis.

Helena R. Zimmermann, PhD

Brain-Specific Repression of AMPKα1 Alleviates Pathophysiology in Alzheimer's Model Mice

Citation: *Journal of Clinical Investigation. 2020 Jul 1;130(7):3511-3527.*

Authors: Zimmermann HR, Yang W, Kasica NP, Zhou X, Wang X, Beckelman BC, Lee J, Furdui CM, Keene CD, Ma T

Summary: This multidisciplinary study, based on human brain samples and mouse models of Alzheimer's disease (AD), indicates an association between dysregulated AMPK signaling and AD pathogenesis. The findings reveal previously unrecognized molecular mechanisms underlying AD, and may provide insights into development of novel therapeutic approaches and biomarkers for AD and related dementia syndromes.

Swapan K. Das, MSc, PhD

Integrative Analysis of Glucometabolic Traits, Adipose Tissue DNA Methylation, and Gene Expression Identifies Epigenetic Regulatory Mechanisms of Insulin Resistance and Obesity in African Americans

Citation: *Diabetes. 2020 Dec;69(12):2779-2793.*

Authors: Sharma NK, Comeau ME, Montoya D, Pellegrini M, Howard TD, Langefeld CD, Das SK

Summary: Applying an integrative multi-omics approach, this study provides evidence for DNA methylation-mediated epigenetic regulation of gene expression at several loci for key adipose tissue transcripts influencing insulin resistance (IR) and obesity in African Americans. Knowledge derived from this study may play an important role in the development of novel therapeutic options that can modify DNA-methylation levels in adipose tissue and prevent IR and thereby reduce progression to Type 2 diabetes.

Michelle M. Marks, MD

Tumour Necrosis Factor-Related Apoptosis-Inducing Ligand (TRAIL) and Receptors in Type 1, Type 2 and Type 17 Inflammation in Cross-Sectional Asthma Study

Citation: *Thorax. 2020 Sep;75(9):808-811.*

Authors: Marks M, Steele C, Moore WC, Meyers DA, Rector B, Ampleford E, Bleecker ER, Hastie AT

Summary: This study examined the role of Tumor Necrosis factor-Related Apoptosis-Inducing Ligand (TRAIL), in either promoting or resolving airway inflammation in asthma. Higher levels of TRAIL were associated with increases in mediators of Type 1, Type 2 and Type 17 inflammation, but also increased expression of TRAIL decoy receptors on airway granulocytes, suggesting that TRAIL apoptotic signal is reduced, and cellular inflammation is prolonged in patients with asthma.

Anthony J. Bleyer, MD, MS

Clinical and Genetic Spectra of Autosomal Dominant Tubulointerstitial Kidney Disease Due to Mutations in UMOD and MUC1

Citation: *Kidney International. 2020 Sep;98(3):717-731.*

Authors: Olinger E, Hofmann P, Kidd K, Dufour I, Belge H, Schaeffer C, Kipp A, Bonny O, Deltas C, Demoulin N, Fehr T, Fuster DG, Gale DP, Goffin E, Hodaňová K, Huynh-Do U, Kistler A, Morelle J, Papagregoriou G, Pirson Y, Sandford R, Sayer JA, Torra R, Venzin C, Venzin R, Vogt B, Živná M, Greka A, Dahan K, Rampoldi L, Kmoch S, Bleyer AJ Sr, Devuyst O

Summary: Autosomal dominant tubulointerstitial kidney disease (ADTKD) is a cause of chronic kidney disease leading to end-stage kidney disease at a median age of 50 years. This study, which involved collaborations among research groups in 10 countries, evaluated 726 patients with mutations in UMOD and MUC1 from 585 families with ADTKD, most of whom were from the Wake Forest registry. The study found that patients with MUC1 mutations had an earlier age of onset of kidney disease and much less frequent gout than families with UMOD mutations.

Suzanne Craft, PhD

Safety, Efficacy, and Feasibility of Intranasal Insulin for the Treatment of Mild Cognitive Impairment and Alzheimer Disease Dementia: A Randomized Clinical Trial

Citation: *JAMA Neurology. 2020 Sep 1;77(9):1099-1109.*

Authors: Craft S, Raman R, Chow TW, Rafii MS, Sun CK, Rissman RA, Donohue MC, Brewer JB, Jenkins C, Harless K, Gessert D, Aisen PS

Summary: This Phase II clinical trial examined the safety and efficacy of a novel therapeutic approach for Alzheimer's disease (AD) that was designed to deliver insulin directly to the brain via intranasal administration with specialized devices. Although results were negative for the primary cohort treated with an actuator device, a secondary cohort utilizing a nebulizer device showed clinically significant improvement in cognition, function and cerebrospinal fluid biomarkers of AD pathology over an 18 month period, providing a strong rationale for further study of this therapeutic approach and underscoring the need to investigate the effectiveness of different devices in delivering insulin to the brain.

Saad Z. Usmani, MD, MBA, FACP

Carfilzomib, Dexamethasone, and Daratumumab versus Carfilzomib and Dexamethasone for Patients with Relapsed or Refractory Multiple Myeloma (CANDOR): Results from a Randomised, Multicentre, Open-Label, Phase 3 Study

Citation: *Lancet. 2020 Jul 18;396(10245):186-197.*

Authors: Dimopoulos M, Quach H, Mateos MV, Landgren O, Leleu X, Siegel D, Weisel K, Yang H, Klippel Z, Zahlten-Kumeli A, Usmani SZ

Summary: Multiple myeloma (MM) is the second most common blood cancer in the US and the most common blood cancer in African Americans. While the use of proteasome inhibitors and lenalidomide have improved outcomes, MM largely remains incurable. With the increasing use of lenalidomide based therapies, there is a need for lenalidomide-sparing regimens at relapse. The CANDOR trial demonstrates the potential efficacy of a lenalidomide-sparing regimen, that includes daratumumab and carfilzomib, in providing a durable response upon relapse. Based on the CANDOR trial results, this regimen was FDA approved on August 20, 2020.

Nilanjan Ghosh, MD, PhD

Association of Reduced-Intensity Conditioning Regimens with Overall Survival Among Patients with Non-Hodgkin Lymphoma Undergoing Allogeneic Transplant

Citation: *JAMA Oncology. 2020 Jul 1;6(7):1011-1018.*

Authors: Ghosh N, Ahmed S, Ahn KW, Khanal M, Litovich C, Aljurf M, Bacher VU, Bredeson C, Epperla N, Farhadfar N, Freytes CO, Ganguly S, Haverkos B, Inwards D, Kamble RT, Lazarus HM, Lekakis L, Murthy HS, Nishihori T, Ramakrishnan P, Rizzieri DA, Yared JA, Kharfan- Dabaja MA, Sureda A, Hamadani M

Summary: This study found that use of a more intense reduced-intensity conditioning and non-myeloablative conditioning regimen for allogeneic hematopoietic cell transplant (HCT) in patients with non-Hodgkin lymphoma should be considered with caution. The findings suggest that use of the more intense regimen (fludarabine and melphalan) may have a negative association with overall survival and may be associated with higher non-relapse mortality than fludarabine and busulfan and a higher risk of graft versus host disease than fludarabine and cyclophosphamide.

Priyesh A. Patel, MD

Association between Systolic Ejection Time and Outcomes in Heart Failure by Ejection Fraction

Citation: *European Journal of Heart Failure. 2020 Jul;22(7):1174-1182.*

Authors: Patel PA, Ambrosy AP, Phelan M, Alenezi F, Chiswell K, Van Dyke MK, Tomfohr J, Honarpour N, Velazquez EJ

Summary: Systolic ejection time (SET) is a simple echocardiographic parameter that is independently associated with hospitalization and survival for patients with heart failure reduced ejection fraction, but not for heart failure preserved ejection fraction. These data suggest that SET, when measured accurately, has an important role in the global assessment of systolic function for HFrEF patients.

Matthew J. Singleton, MD, MBE, MHS, MSc

Effect of Intensive Glycemic and Blood Pressure Control on QT Prolongation in Diabetes: The ACCORD Trial

Citation: *Diabetes. 2020 Oct;69(10):2186-2193.*

Authors: Singleton MJ, Soliman EZ, Bertoni AG, Whalen SP, Bhave PD, Yeboah J

Summary: The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial found that intensive glycemic control, compared to standard control, was associated with increased mortality. Because intensive glycemic control is associated with QT prolongation, it has been proposed that the excess mortality in ACCORD may be secondary to QT prolongation leading to lethal ventricular arrhythmias. The current study examined serial QT measurements in ACCORD study participants and found that intensive glycemic control did not lead to an increased risk of QT prolongation. Thus, the increased mortality observed in the intensive glycemic control arm in the ACCORD trial is not explained by QT prolongation.

Dermot M. Phelan, MD, PhD, FASE, FACC

Screening of Potential Cardiac Involvement in Competitive Athletes Recovering from COVID-19: An Expert Consensus Statement

Citation: *JACC Cardiovascular Imaging. 2020 Dec;13(12):2635-2652.*

Authors: Phelan D, Kim JH, Elliott MD, Wasfy MM, Cremer P, Johri AM, Emery MS, Sengupta PP, Sharma S, Martinez MW, La Gerche A

Summary: COVID-19 related cardiac injury may have unique implications for athletes, given concern that exercise, during the acute phase of myocardial inflammation, may exacerbate injury and precipitate malignant arrhythmias. This study proposes a framework for the role of multi-modality imaging in the evaluation of athletes post COVID-19, highlighting the unique challenges posed in distinguishing athletic cardiac remodeling from subclinical cardiac disease and providing diagnostic "red flags" that raise the suspicion of pathology.

B. Hadley Wilson, MD, FACC

New ACC Global Heart Attack Treatment Initiative: Improving STEMI Care Worldwide

Citation: *Journal of the American College of Cardiology. 2020 Apr 7;75(13):1605-1608.*

Authors: Levenson B, Herrera C, Wilson BH

Summary: With over 3 million ST elevation myocardial infarctions (STEMIs) occurring annually in low- and middle-income countries, the American College of Cardiology launched the Global Heart Attack Initiative in October 2019. To date, the initiative has prospectively enrolled more than 2,000 STEMI patients in 18 sites in 13 nations on five continents. Interim findings include significant reductions in transportation time, arrest on arrival, first medical contact to balloon, and adherence to Guideline-Directed Medical Therapy all of which are known to improve outcomes in acute myocardial infarction.

Michael V. Rocco, MD, MSCE

Effects of Intensive Systolic Blood Pressure Control on All-Cause Hospitalizations

Citation: *Hypertension. 2020 Dec;76(6):1717-1724.*

Authors: Rocco MV, Comeau ME, Marion MC, Freedman BI, Hawfield AT, Langefeld CD; SPRINT Research Group

Summary: The SPRINT (Systolic Blood Pressure Intervention Trial) demonstrated that intensive blood pressure control (systolic blood pressure of less than 120 mm Hg compared with systolic blood pressure of less than 140 mm Hg) was associated with a significant decrease in both cardiovascular events and all-cause mortality. In this manuscript, it was demonstrated that intensive blood pressure control does not lead to adverse events that result in an increased rate of non-cardiovascular hospitalizations.

David P. Miller, Jr., MD, MS, FACP

Security and Privacy Risks Associated With Adult Patient Portal Accounts in US Hospitals

Citation: *JAMA Internal Medicine. 2020 Jun 1;180(6):845-849.*

Authors: Latulipe C, Mazumder SF, Wilson RKW, Talton JW, Bertoni AG, Quandt SA, Arcury TA, Miller DP Jr

Summary: Patient portals can help caregivers better manage care for older patients, but how caregivers access the patient portal could threaten patient security and privacy. In this national cross-sectional study of 102 US hospitals, almost half of surveyed hospital personnel recommended password sharing and few hospitals enabled patients to limit the types of information seen by those with proxy access.

Kranthi Sitammagari, MD, FACP, CHCQM-PHYADV

Insights from Rapid Deployment of a "Virtual Hospital" as Standard Care During the COVID-19 Pandemic

Citation: *Annals of Internal Medicine. 2021 Feb;174(2):192-199. Epub 2020 Nov 11.*

Authors: Sitammagari K, Murphy S, Kowalkowski M, Chou SH, Sullivan M, Taylor S, Kearns J, Batchelor T, Rivet C, Hole C, Hinson T, McCreary P, Brown R, Dunn T, Neuwirth Z, McWilliams A

Summary: This paper described how a multidisciplinary care team within a Learning Health System developed and rapidly deployed a virtual hospital program to increase the capacity to provide hospital-level services to patients with COVID-19 during the early chaotic days of the pandemic. The paper outlines implementation lessons and a framework for leveraging a virtual platform, health IT, and data-informed decision making to help overcome the challenges inherent to implementing a novel care model, while also sharing preliminary results on the first 1477 COVID-19 patients.


Wake Forest®
School of Medicine


Wake Forest®
Baptist Health


Atrium Health