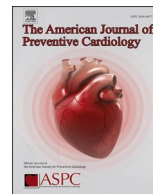


Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

# American Journal of Preventive Cardiology

journal homepage: [www.journals.elsevier.com/american-journal-of-preventive-cardiology](http://www.journals.elsevier.com/american-journal-of-preventive-cardiology)

State-of-the-Art Review

## American society for preventive cardiology 2024 cardiovascular disease prevention: Highlights and key sessions



Akhil A. Chandra<sup>a,†</sup>, Carlos Espiche<sup>a,†</sup>, Maisha Maliha<sup>b</sup>, Salim S Virani<sup>c</sup>, Roger S Blumenthal<sup>d</sup>,  
Fatima Rodriguez<sup>e</sup>, Nathan D Wong<sup>f</sup>, Martha Gulati<sup>g</sup>, Leandro Slipczuk<sup>a,\*</sup>,  
Michael D Shapiro<sup>h</sup>

<sup>a</sup> Division of Cardiology, Montefiore Health System/Albert Einstein College of Medicine, New York, NY, USA<sup>b</sup> Division of Medicine, Jacobi Medical Center, Bronx, NY, USA<sup>c</sup> Aga Khan University, Karachi, Pakistan<sup>d</sup> The Ciccarone Center for the Prevention of Cardiovascular Disease Johns Hopkins University School of Medicine, Baltimore, MD, United States<sup>e</sup> Division of Cardiovascular Medicine and the Cardiovascular Institute, Stanford University School of Medicine, Stanford, CA, United States<sup>f</sup> Heart Disease Prevention Program, Division of Cardiology, Department of Medicine, University of California, Irvine, CA, United States<sup>g</sup> Barbra Streisand Women's Heart Center, Smidt Heart Institute, Cedars-Sinai Medical Center, 127 S San Vicente Blvd-AHSP, A3100, Los Angeles, CA 90048, USA<sup>h</sup> Division of Cardiology, Wake Forest University, Winston-Salem, NC, USA

**Abbreviations:** ACC, American College of Cardiology; ACEi, Angiotensin-converting enzyme inhibitor; ACS, Acute coronary syndrome; AHA, American Heart Association; AI, Artificial intelligence; ARB, Angiotensin receptor blocker; ARR, Absolute risk reduction; ASCVD, atherosclerotic cardiovascular disease; ASPC, American Society for Preventive Cardiology; ApoB, Apolipoprotein B; AU, Agatston units; BMI, Body mass index; CAC, Coronary artery calcium; CAD, Coronary artery disease; CARDIA, The Coronary Artery Risk Development in Young Adults; CCTA, Coronary computed tomography angiography; CHD, Congenital heart disease; CI, Confidence Interval; CKD, Chronic kidney disease; CKM, Cardiovascular-kidney-metabolic; CONFIRM, Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter; CVD, Cardiovascular disease; EPA, Eicosapentaenoic acid; FDG, Fluorodeoxyglucose; GLP-1, Glucagon-like peptide-1; GLP-1 RA, Glucagon-like peptide-1 receptor agonists; HR, Hazard ratio; HRP, High-risk plaque; hsCRP, High-sensitivity C-reactive protein; JAK, Janus kinase; LAP, Low attenuation plaque; LDL-C, low-density lipoprotein-cholesterol; Lp(a), Lipoprotein(a); MACE, Major adverse cardiovascular events; MBDA, Multi-biomarker disease activity score; MESA, Multi-Ethnic Study of Atherosclerosis Study; MI, Myocardial infarction; MRI, Myocardial resonance Imaging; MTX, Methotrexate; NO, Nitric oxide; NIH, National Institute of Health; NSTEMI, non-ST elevation MI; OMT, Optimal medical therapy; PAD, Peripheral artery disease; PCSK9i, Proprotein convertase subtilisin/kexin type 9 inhibitors; PESA, Progression of Early Subclinical Atherosclerosis; OR, Odds ratio; RA, Rheumatoid arthritis; RNA, Ribonucleic acid; RC, Reduced carbohydrate; RF, Reduced fat; SELECT, Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes; SCCT, Society of Cardiovascular Computed Tomography; SGLT2, Sodium-glucose cotransporter-2; SLE, Systemic lupus erythematosus; STEMI, ST-elevation myocardial infarction; TAC, Thoracic aorta calcification; T2DM, Type 2 diabetes mellitus; TNFi, Tumor necrosis factor inhibitors; WARRIOR Trial, Women's Ischemia Treatment Reduces Events in Non-OstRuctive CAD Trial; WISE, Women's Ischemia Syndrome Evaluation.

\* Corresponding author at: Montefiore Medical Center, Moses Campus, 111 E 210th St, Bronx, NY, USA.

E-mail address: [lslipczukb@montefiore.org](mailto:lslipczukb@montefiore.org) (L. Slipczuk).

† co-first authors

<https://doi.org/10.1016/j.ajpc.2024.100919>

Available online 15 December 2024

2666-6677/© 2024 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## GRAPHICAL ABSTRACT



## ARTICLE INFO

## Keywords:

Preventive cardiology  
Lipids  
Precision medicine

## ABSTRACT

Groundbreaking strategies for preventive cardiology were showcased at the 2024 American Society for Preventive Cardiology (ASPC) Congress on Cardiovascular Disease (CVD) Prevention held in Salt Lake City, Utah, from August 2nd to 4th, 2024. The event featured 69 moderators and 13 scientific sessions comprised of 98 topics, 36 satellite events, 133 poster presentations, and 27 lifestyle classes.

The conference highlighted innovative strategies focused on integrating cardiovascular, kidney, and metabolic health, presenting a cohesive approach for managing complex, interrelated conditions. Pivotal studies have addressed the role of lipid-lowering therapies, the benefits of early statin initiation, and the importance of precision medicine in preventing CVD.

The ASPC's emphasis on translating this research into practical clinical tools has the potential to revolutionize preventive care strategies, making strides toward reducing the burden of CVD globally and improving long-term patient outcomes through personalized and early intervention approaches.

## 1. Introduction

This article aims to present the latest data and findings from the 2024 American Society for Preventive Cardiology (ASPC) Congress on Cardiovascular Disease (CVD) Prevention, held in Salt Lake City, Utah, from August 2nd to 4th, 2024. By highlighting key studies and discussions from this national conference, this review seeks to convey the most innovative approaches in preventive healthcare to the greater cardiology community. The conference underscored the importance of translating groundbreaking research into practical strategies that can advance clinical care and improve patient outcomes across the field of cardiology.

## 2. Opening session

### 2.1. Honorary fellow award lecture: lipid lowering 2024 and beyond (Christopher Cannon, MD)

The history behind low-density lipoprotein-cholesterol (LDL-C) associated risk and lowering methods is vast. Yet, there is no consensus on target values for patient groups with elevated LDL-C [1]. The determination of LDL-C targets for patients based on risk stratification has been studied, specifically with regards to initiating medical therapy [2]. However, viewpoints against relying on LDL-C targets do exist [3]. Current primary prevention guidelines recommend initiation of statin therapy using risk assessment tools that heavily rely on age [4]. Such alternative viewpoints also include the unknown magnitude of additional atherosclerotic cardiovascular disease (ASCVD) risk reduction with one target value compared to another and a known risk continuum over LDL-C target goals.

IMPROVE-IT, a randomized trial that has improved understanding of

lipid-lowering therapies, has been key to understanding lipid-lowering therapy in adults with a recent acute coronary syndrome (ACS). IMPROVE-IT randomized 18,144 patients with ACS to simvastatin alone or ezetimibe/simvastatin with a median follow-up of 6 years. Inclusion criteria included men and women >50 years old with a maximum LDL-C level of 125 mg/dL in patients not receiving long-term lipid-lowering therapy and 100 mg/dL in patients receiving lipid-lowering therapy. At 1 year follow-up, the mean LDL-C level was 69.9 mg/dL in the simvastatin-monotherapy group and 53.2 mg/dL in the simvastatin–ezetimibe group ( $p < 0.001$ ). IMPROVE-IT further noted a statistically significant lower rate of cardiovascular death/nonfatal myocardial infarction/coronary revascularization/stroke (Hazard Ratio (HR) 0.94, 95 % Confidence Interval (CI) 0.89–0.99,  $p = 0.016$ ) in the simvastatin/ezetimibe group as compared to simvastatin alone (2572 events, 32.7 % vs 2742 events, 34.7 %), demonstrating superiority of an LDL-C lowering strategy with statin and ezetimibe combination therapy [5].

Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) monoclonal antibodies have further emerged as lipid-lowering therapy options, with data showing very low LDL-C values confer a benefit in secondary prevention. In the FOURIER study, a randomized study of 27,564 patients with ASCVD and LDL-C  $\geq 70$  mg/dL or non-high-density lipoprotein cholesterol (non-HDL-C)  $> 100$  mg/dL on statin therapy, there was a statistically lower risk of CVD, acute coronary syndrome (ACS), stroke or coronary revascularization in the PCSK9i group (evolocumab) as compared with placebo (14.6 vs 12.6, HR 0.85 95 % CI 0.79–0.92,  $p < 0.0001$ ) [6]. Of note, at 48 weeks, LDL-C was reduced to 70 mg/dL or lower in 87 % of the patients in the evolocumab group compared to 18 % in the placebo group. Moreover, when combined with statin therapy, PCSK9i use was noted to significantly reduce the percent of atheroma volume ( $p < 0.001$ ) [7]. The ODYSSEY outcomes trial evaluated alirocumab, a PCSK9i monoclonal antibody, in 18,924

patients with recent ACS already on high-intensity statins, LDL-C >70 mg/dL, non-HDL-C >100 mg/dL or apolipoprotein B >80 mg/dL. Alirucumab significantly reduced the risk of major adverse cardiovascular events (MACE, HR 0.85, 95 % CI 0.78–0.93,  $p < 0.001$ ), and lowered all-cause mortality compared to placebo (3.5 % in treatment arm vs 4.1 % in placebo, (HR 0.85, 95 % CI 0.73–0.98) [8]. Importantly, both PCSK9i monoclonal antibodies demonstrated further decrease of MACE even at very low levels of LDL-C. These findings suggest that an approach of “the lower, the better” for LDL-C lowering, as opposed to a purely target-driven one, should be considered in secondary prevention.

Bempedoic acid has recently gained traction as a lipid-lowering therapy, particularly in statin-intolerant patients. A randomized double-blind trial by Nissen et al. involving 13,970 patients unable or unwilling to take statin, demonstrated that bempedoic acid resulted in a 21.1 % greater reduction in LDL-C compared to placebo and significantly decreased the risk of MACE [819 patients (11.7 %) vs. 927 (13.3 %); HR 0.87, 95 % CI, 0.79–0.96,  $p = 0.004$ ). However, its use was associated with increased rates of gout and cholelithiasis [9]. As a result, it has emerged as a viable alternative for lowering MACE risk in statin-intolerant individuals, complementing other therapeutic strategies for high-risk patients.

Inclisiran, a small interfering ribonucleic acid (RNA) therapy targeting hepatic PCSK9 synthesis, was also discovered to achieve sustained LDL-C reduction with biannual dosing. In one trial by Ray et al. in 2017, inclisiran demonstrated a 35.5 % to 52.6 % reduction in LDL-C in patients with ASCVD or equivalent risk, compared to placebo ( $p < 0.001$ ) [10]. The ORION-10 and ORION-11 trials further demonstrated LDL-C reductions of about 52.3 % (95 % CI 48.8 %–55.7 %) and 49.9 % (95 % CI 46.6 %–53.1 %), respectively over 510 days with inclisiran administered biannually, with mild injection-site reactions as the primary adverse event [11]. Overall, LDL-C reductions of approximately 50 % were achieved with inclisiran. Future advancements in lipid-lowering therapies are likely to focus on long-acting PCSK9i, easier administration routes (such as oral) and novel small molecule inhibitors [12].

## 2.2. Joseph Stokes III, MD pioneer in prevention award lecture (Sergio Fazio, MD, PhD, FASPC)

The ASPC faces challenges in establishing preventive cardiology as a distinct subspecialty. A key challenge is functional overlap with general cardiology, which often views prevention as part of its core practice, and from organizations such as the National Lipid Association and Cardiometabolic Health Alliance. However, the ASPC’s strength lies in its specific focus on cardiovascular health, setting it apart from groups concentrating on lipids or metabolic conditions. With a membership primarily comprising cardiologists and cardiovascular professionals, the ASPC is well-positioned to lead in preventive cardiology. As part of the strategic framework for this process, a proposal was made for a comprehensive training and certification process to ensure nationwide and global adoption of preventive cardiology practices. Advocacy for cost regulation and insurance coverage of essential tests was also emphasized to enhance accessibility.

## 2.3. The nanette wenger award lecture: where are we now? – From WISE to Chest Pain guidelines and improving CVD care for Women (Noel Bairey-Merz, MD)

Non-obstructive coronary disease is more prevalent in women than in men, particularly in the context of ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI). Women and non-White individuals with chest pain are also more likely to have non-obstructive coronary artery disease (CAD) [13]. This is thought to be linked to sex/ethnicity-specific conditions such as post-menopause, low estrogen levels, and polycystic ovarian syndrome, which elevate cardiovascular risk factors like hypertension, obesity, and hyperlipidemia, leading to coronary endothelial dysfunction [14]. Pharmacologic

interventions from studies such as WISE (Women’s Ischemia Syndrome Evaluation) were discussed at ASPC 2024 and noted to have advanced existing knowledge regarding this topic [15].

There is particular interest in the recently completed WARRIOR Trial (Women’s Ischemia Treatment Reduces Events in Non-Obstructive Coronary Artery Disease Trial) which randomized 4422 women with symptomatic, non-obstructive CAD to intensive medical therapy (on a statin and an angiotensin-converting enzyme inhibitor (ACEi)/angiotensin receptor blocker (ARB)) vs usual care to study the reduction in MACE [16]. Overall, observational studies have demonstrated myocardial ischemia with non-obstructive coronary arteries is more common in women, and mechanisms include traditional cardiac and sex-specific risk factors. Interventional trials are ongoing, and translational work is crucial to success in therapeutic development.

## 2.4. American journal of preventative cardiology (AJPC) Editor’s update and Top 5 papers in prevention (Nathan D. Wong, PhD, MASPC)

An update of the AJPC was presented. Through July 2024, submissions for the year have exceeded all submissions during 2023, and there has also been a more selective process required for article acceptance. With the more significant number of submissions, processing has increased slightly to 7.4 weeks for the first decision. Of note, while many journals saw a decrease in their impact factor, the AJPC’s impact factor remained strong, increasing slightly to 4.3. Moreover, the AJPC currently ranks 45 out of 220 (79.8th percentile) worldwide after only 4½ years of publication. AJPC is frequently cited by the *Journal of the American College of Cardiology*, *Circulation*, and the *New England Journal of Medicine*. The Journal’s editorial board is diverse, with 77 editorial board members representing 20 countries, 27 % being women, similar to the 29 % of cardiovascular authors being women; however, the Journal continues to seek greater diversity in both its editorial board as well as in geographic distribution of its published articles. The top 5 editorial picks for articles related to preventive cardiology (among all journals) included:

### 2.4.1. Semaglutide and Cardiovascular outcomes in obesity without diabetes (SELECT)[17]

The SELECT trial was designed to evaluate whether adding semaglutide to the standard of care was more effective than a placebo in reducing MACE among patients with obesity and pre-existing CVD who did not have type 2 diabetes (T2DM). The trial included participants who met the following inclusion criteria: 1) 45 years or older, 2) Body Mass Index (BMI)  $\geq 27$  kg/m<sup>2</sup>, and 3) Established CVD. The trial found a statistically significant reduction in the primary endpoint (MACE, CV death, nonfatal Myocardial Infarction (MI), and nonfatal stroke) with semaglutide (HR 0.80, Absolute Risk Reduction (ARR) 1.5 %, 95 % CI 0.72–0.90,  $p < 0.001$ ). There was also a notable reduction in cardiovascular death (HR 0.85, ARR 0.5 %, 95 % CI 0.71–1.01,  $p = 0.07$ ), heart failure composite endpoint (HR 0.82, ARR 0.7 %, 95 % CI 0.71–0.96), and death from any cause (HR 0.81, ARR 0.9 %, 95 % CI 0.71–0.93). Notably, there was also a 73 % reduction in the risk of incident T2DM. Thus, over a mean follow-up period of 39.8 months, weekly subcutaneous injections of 2.4 mg semaglutide were superior to placebo in reducing composite cardiovascular outcomes and its components among patients with pre-existing CVD and overweight or obesity but without T2DM.

### 2.4.2. Cardiovascular-kidney-metabolic health: a presidential advisory from the American heart association[18]

Cardiovascular-Kidney-Metabolic (CKM) Health refers to the interconnected pathophysiology of heart disease, kidney disease, T2DM, and obesity, which collectively contribute to poor health outcomes. CKM health is categorized into stages, each with specific treatment guidelines, as outlined by the American Heart Association (AHA).

- Stage 0 (No CKM Risk Factors): Focuses on prevention through school and family-based interventions to promote healthy lifestyles.
- Stage 1 (Excess or Dysfunctional Adiposity): Targets weight loss to address obesity and its associated risks.
- Stage 2 [Metabolic Risk Factors or Chronic Kidney Disease (CKD)]: Involves managing cardiovascular risk factors, such as hypertension and T2DM, to prevent disease progression.
- Stage 3 (Subclinical Cardiovascular Disease in CKM Syndrome): Utilizes medications like statins, ACEi, and beta-blockers to manage subclinical cardiovascular disease.
- Stage 4 (Clinical Cardiovascular Disease in CKM Syndrome): Requires intensive pharmacologic therapies to manage advanced cardiovascular disease and its complications, including kidney failure.

This structured approach emphasizes early intervention and tailored treatment strategies to improve outcomes across the CKM health spectrum.

#### 2.4.3. When does a coronary calcium score equate to secondary prevention [19]?

This study involved 4949 patients from the multinational Phase 1 and Phase 2 CONFIRM (Coronary Computed Tomography Angiography (CCTA) Evaluation for Clinical Outcomes: An International Multicenter) registry, with a mean age of 57.6 years and 56.0 % being male. The authors performed a cohort study comparing event rates of patients with established ASCVD (documented history of MI, stroke, or peripheral artery disease (PAD)) to event rates in persons with no history of ASCVD and known coronary artery calcium scores (CAC) to ascertain at what level elevated CAC equates to the risk associated with existing ASCVD.

The study assessed outcomes, including all-cause mortality and MACE, over a median follow-up period of 4 years. Participants with a CAC >300 Agatston Units (AU) had a risk of MACE that was equivalent to those with pre-existing ASCVD who were already undergoing treatment. This finding supports the concept of a risk continuum between primary and secondary prevention, strongly supporting the use of CAC for risk stratification and consideration of aggressive preventive therapies for those with CAC >300 AU, even in the absence of clinical ASCVD.

#### 2.4.4. High Lipoprotein(a): actionable strategies for risk assessment and mitigation[20]

This review discussed the clinical guidelines and consensus statements from various national and international cardiovascular organizations on Lipoprotein(a) [Lp(a)] detection and treatment strategies. The report highlighted that multiple societies recommend Lp(a) testing, recognizing that elevated Lp(a) levels are causally linked to ASCVD, calcific aortic stenosis, and may contribute to thrombotic conditions. Additionally, identifying high Lp(a) levels can help clinicians tailor interventions to reduce cardiovascular risk factors more effectively. Additional research focusing on non-White populations and therapeutic outcome trials is necessary and currently underway, with results anticipated in the coming years.

#### 2.4.5. Atherosclerotic coronary plaque regression from lipid-lowering therapies: a meta-analysis and meta regression[21]

This study assessed the impact of various lipid-lowering therapies on plaque regression, using multiple markers and conducting subgroup analyses based on the type of therapy and post-treatment LDL-C levels. The therapies evaluated included low and high-intensity statins, eicosapentaenoic acid (EPA), ezetimibe, and PCSK9i. The primary outcomes measured were changes in percent atheroma volume, plaque lumen volume, and vessel volume. Lipid-lowering therapies resulted in a significant reduction in total atheroma volume, with a mean decrease of  $-5.84 \text{ mm}^3$  ( $p < 0.001$ ), and in percent atheroma volume, with a mean reduction of  $-1.10 \%$  ( $p < 0.001$ ). Significant plaque regression was observed particularly with high-intensity statins, low-intensity statins combined with ezetimibe, lower-intensity statins combined with EPA,

and PCSK9i. High-intensity statins were the most effective, driving the largest reduction in total atheroma volume ( $-7.60 \text{ mm}^3$ ,  $p < 0.01$ ).

### 3. Cohort Studies & population health

#### 3.1. Lessons from the multi-ethnic study of atherosclerosis study (MESA, Khurram Nasir, MD, MPH, FASPC)

Studies utilizing MESA have offered important insights into CVD prevention. One such study was conducted by Detrano et al., which included 6722 men and women over a mean 3.8-year period to learn whether CAC predicted coronary heart disease [22]. The study found that across four racial and ethnic groups, compared to participants with no CAC, the adjusted risk of a coronary event was increased by a factor of 7.8 among participants with CAC between 101 and 300 AU and by a factor of 9.7 among participants with scores > 300 AU ( $p < 0.001$  for both comparisons). Based on these findings, the 2010 American College of Cardiology (ACC)/AHA Guidelines recommend using CAC to assess the burden of atherosclerosis in patients with borderline or intermediate ASCVD risk when cardiovascular risk remains uncertain [23].

#### 3.2. Lessons from progression of early subclinical atherosclerosis (PESA, Ines Garcia Lunar, MD, PhD)

The PESA study, a longitudinal investigation involving 4200 participants (1500 women) with over 16 years of follow-up, included asymptomatic individuals free of clinical CVD who underwent screening for subclinical atherosclerosis with ultrasound and CAC [24]. The study has advanced to include sophisticated imaging techniques, such as Positron Emission Tomography/Magnetic Resonance Imaging (MRI) and cardiac MRI, for nearly 800 participants. Key findings from PESA include the high prevalence and rapid progression of subclinical atherosclerosis among middle-aged subjects.

Additionally, PESA has revealed that plaque in the carotid or femoral arteries is present in approximately 40 % of participants with a zero CAC. Looking ahead, the principal investigators plan to conduct a 5-year randomized trial. This trial will involve 4184 asymptomatic middle-aged patients aged 20–39 with LDL-C levels  $\geq 70 \text{ mg/dL}$  and no history of CVD, comparing active treatment (including statins, metformin, Sodium-glucose cotransporter-2 inhibitors (SGLT2i), etc.) against standard care (defined as annual follow-up). The objective of this trial is to determine whether early treatment of asymptomatic subclinical atherosclerosis in this patient population may result in better long-term outcomes [25,26].

#### 3.3. Lessons from the coronary artery risk development in young adults (CARDIA, Sadiya Khan, MD, MSc)

The CARDIA study began enrollment in 1985 with an initial group of 5115 Black and White men and women aged 18–30 years and has examined the development of clinical and subclinical CVD [27]. The study has been broken into 3 Phases: Phase 1 (Lifestyle, Determinants of Future Risk), Phase 2 (Subclinical Disease) and Phase 3 (Emerging Events). A key finding from the CARDIA study is that cardiac risk factors present before age 35 are significant predictors and potential targets for preventing heart failure across different racial groups [28]. The study has further documented the detrimental impact of healthcare disparities across racial groups and delineated drivers of racial inequality, including factors such as lifestyle, depression, and socioeconomic background. These healthcare disparities have been linked to premature CVD [29,30]. Recently, CARDIA has evaluated the impact of a history of gestational diabetes on CAC in women. Women with a history of gestational diabetes have a two-fold increased risk of CAC across all subsequent levels of glucose tolerance [31].

#### 4. Innovative strategies in CVD prevention

ASPC featured a discussion panel about innovative strategies for CVD prevention. This included lectures on the experience of the Korean Lipid and Atherosclerosis Society for CVD prevention, advances in lipid management for atherosclerosis prevention, and advancements in preventive cardiology (including genomics and precision medicine).

##### 4.1. Korean lipid and atherosclerosis society and korean society for preventive cardiology (Hyeon Chang Kim, MD, PhD)

In the initial discussion of this topic, it was shown that mortality linked to CVD has been declining over recent years. However, the incidence of MI and stroke varies according to age groups and countries. The Korean experience highlighted how leveraging big data for real-time collection has significantly influenced CVD prevention efforts [32]. This approach is exemplified by the National Health Insurance (NHI) of Korea, which enables rapid population-level analysis and facilitates large-scale interventions and recommendations. However, despite its promising potential, this database has limitations, including biases in data collection, a lack of deep phenotyping, and the exclusion of non-covered services and treatment outcomes [33].

##### 4.2. LDL-C goals in cardiovascular prevention: IMPROVE-IT and RACING trials (Jung-Joon Cha, MD, PhD)

Aggressive LDL-C lowering in high-risk patients is an area of active research [34]. An important topic discussed was the importance of primary and secondary prevention in the Korean LDL-C treatment algorithm [2,35]. However, gaps persist in achieving treatment goals, potentially due to concerns about the side effects of high-intensity statins in the Asian population [36,37].

Ezetimibe has emerged as an alternative therapy to tackle these side-effects. The effects of ezetimibe combined with moderate-intensity statins (as opposed to high-intensity statins) are particularly notable while offering a safer drug profile [38,39]. RACING, a randomized non-inferiority trial, included those with ASCVD receiving moderate-intensity statin with ezetimibe (rosuvastatin 10 mg with ezetimibe 10 mg) vs. high-intensity statin monotherapy (rosuvastatin 20 mg) and showed noninferiority among both types of treatment, supporting this concept [40].

##### 4.3. Genetic approach of the cardiovascular prevention medicine (Michael Honigberg, MD, MPP)

Precision medicine is defined as an approach to cardiovascular preventive medicine that considers a person's genetics, lifestyle, and exposures as determinants of cardiovascular health and disease phenotypes [41]. Genetics play a critical role in diseases such as familial hypercholesterolemia and various cardiomyopathies [42]. The role of genetics in CVD has been increasingly recognized, as many genomic regions linked to CAD are not associated with traditional risk factors, underscoring the need for deeper biological exploration [43]. Genomics can be a helpful tool when it is correlated with conventional factors [44] and risk scoring, including cross-ancestry generalizability [43,45].

Further, proteomic analyses are being utilized to predict ASCVD risk across various cardiovascular conditions, marking a significant advancement in precision medicine [46,47]. Advanced machine-learning techniques are being used to identify ASCVD risk through imaging modalities such as CT and chest X-rays, allowing earlier and more accurate diagnosis [47,48]. In this way, precision medicine is increasingly being informed by polygenic scores, multi-omic markers, machine learning for opportunistic risk identification, and personalized care strategies, showing a promising future in CVD prevention.

#### 5. Advances in obesity management: integrating glucagon-like peptide-1-based strategies into clinical practice (Ann Marie Navar, MD, PhD, FASPC and Ashish Sarraju, MD)

This session provided a comprehensive exploration of advances in obesity care, mainly focusing on the integration of Glucagon-like Peptide-1 receptor agonists (GLP1 RA) into clinical practice. The discussions began with an insightful review of the historical context of obesity management, highlighting the limitations of traditional methods and the emergence of pharmacological interventions that target the metabolic processes contributing to obesity.

##### 5.1. Look AHEAD research group (Ambarish Pandey, MD)

Novel data on obesity trends have emphasized the increasing prevalence of obesity and its direct correlation with heightened CVD. Data from the Look AHEAD Research Group (2013, 2016) has provided a foundational understanding of the long-term implications of obesity on cardiovascular health [49]. The group studied over 5000 patients with T2DM with BMI > 25 kg/m<sup>2</sup>, aged between 45 and 75 years old, and demonstrated that lifestyle modification was associated with a significant reduction in weight. It was also noted that participants who achieved a 10 % reduction in body weight experienced a significant decrease in MACE.

GLP-1 RA such as semaglutide and tirzepatide have shown promising results in reducing not only weight but also the incidence of cardiovascular events [50–52]. In one retrospective cohort study completed by Chuang et al. of 14,834 patients with T2DM treated with tirzepatide vs. 125,474 patients with T2DM treated with GLP-1 RA, tirzepatide treatment was associated with lower all-cause mortality (HR 0.58, 95 % CI 0.45–0.75) and MACE (HR 0.80, 95 % CI 0.71–0.91) compared with GLP-1 RA [53].

Although emerging data on tirzepatide is available, the SURPASS CVOT is ongoing and anticipated to conclude in late 2024. SURPASS CVOT is a randomized, double-blind study including 13, 299 participants from over 30 countries [54]. The inclusion criteria for this study was men and women over 40 years old with T2DM (HbA1C ≥ 7 % and ≤ 10.5 %) and BMI ≥ 25 kg/m<sup>2</sup> associated with either documented CAD, cerebrovascular disease or PAD. The objective of the study is to compare the effect of weekly tirzepatide (dose-escalated up to 15 mg) with once-weekly dulaglutide (1.5 mg) in patients with T2DM and established ASCVD. This would be the first trial comparing GLP-1 RA with a dual GLP1 RA/gastric inhibitory peptide (GIP) agonists in participants with T2DM and established ASCVD.

Next-generation therapies, such as GLP-1 co-agonists and triple agonists, are poised to offer broader cardiometabolic benefits. They are currently undergoing rigorous clinical trials to evaluate their efficacy and safety on a broader population [52,55].

##### 5.2. LEADER and SUSTAIN: liraglutide and semaglutide (Petra Zubin Maslov, MD, PhD)

The LEADER trial investigated the effects of liraglutide in patients with T2DM at high cardiovascular risk [56]. This trial demonstrated a significant reduction in MACE, marking a milestone in the management of T2DM with cardiovascular comorbidities. Over 9000 patients were divided into two cohorts (liraglutide vs placebo) and followed for 3.8 years. This study observed that patients taking liraglutide experienced fewer deaths from cardiovascular causes compared to those receiving a placebo. Additionally, there was a non-significant reduction in the incidence of non-fatal strokes, nonfatal myocardial infarctions (MI), and hospitalizations for heart failure.

The SUSTAIN-6 trial evaluated semaglutide in over 3000 patients with T2DM who were randomized to receive once-weekly semaglutide or placebo over 104 weeks. The trial demonstrated a significantly lower rate of cardiovascular death, non-fatal MI, and non-fatal stroke among

patients receiving semaglutide compared to placebo, reinforcing the role of GLP-1 RA in reducing cardiovascular risk [57].

Trials such as SURMOUNT and PIONEER have shown GLP-1 RA can lead to significant reductions in systolic blood pressure, primarily through weight loss [55,58,59]. This finding is particularly relevant given the high prevalence of hypertension secondary to obesity in the US [55,60].

## 6. Society of computed tomography at the aspc congress (Sneha Shah Jain, MD and Khurram Nasir, MD, MPH, FASPC)

The Society of Cardiovascular Computed Tomography (SCCT) session at the ASPC Congress emphasized the critical role of cardiac CT in CVD prevention. The session explored its importance in the early detection of CAD and the evaluation of plaque characteristics and high-risk features. Discussions also focused on the integration of cardiac CT into real-world preventive cardiology applications. The session finally examined emerging technologies in cardiac CT and their potential to transform preventive cardiology.

### 6.1. Revolutionizing risk stratification: the role of cardiac CT in early detection of CAD (Maros Ferencik, MD, PhD, MCR)

CCTA is a tool that can detect obstructive and non-obstructive CAD in the early stages of the disease [61]. The diagnostic accuracy was validated by Knuuti et al [62], in a meta-analysis involving 132 studies and 28,664 patients; the study found a high diagnostic accuracy with an area under the curve of 0.72 in comparison with functional studies of 0.64 in predicting cardiovascular events. The PROMISE trial corroborates this data, showing that CCTA can better predict cardiovascular events in patients with non-obstructive CAD compared to functional testing methods [63]. The PARADIGM study provided crucial data on the impact of statins on plaque volume, showcasing examples where a CCTA-driven strategy led to significant reductions in total and non-calcified plaque volumes, typically accompanied by an increase in calcified plaque, an indicator of plaque stabilization [64].

### 6.2. Beyond lumens: cardiac CT for assessing plaque characteristics and vulnerability (Damini Dey, PhD)

Common high-risk plaque (HRP) features include low-attenuation plaque (LAP), positive remodeling, and the napkin-ring sign which are all associated with MACE. The SCOT-HEART and PROMISE trials demonstrated that many patients who experienced MACE did not have visually assessed HRP, underscoring the challenge in predicting which individual plaques may lead to ACS [65]. Quantitative coronary plaque analysis aids in this risk stratification. Data from the SCOT-HEART showed that patients with a higher burden of LAP are almost five times more likely to experience MI [51]. The development of artificial intelligence (AI) and deep learning has reduced the computation time of quantitative plaque analysis to 5.6 seconds from 25.7 minutes, thus revolutionizing coronary plaque analysis [66,67].

### 6.3. Integrating cardiac CT in preventive cardiology: guidelines and real-world applications (Ron Blankstein, MD, FASPC)

Although primarily recommended in patients with borderline or intermediate 10-year ASCVD risk, CAC scoring shows significant prognostic utility in low-risk individuals with an elevated Lp(a) or strong family history [68]. CCTA is increasingly recognized for effective assessment in selected asymptomatic individuals, particularly in those at high risk of noncalcified plaque, and for monitoring the effect of preventive therapies [68]. Data on patient with sequential CCTA showed an independent association between Lp(a) >125 nmol/L and increased plaque volume, the presence of LAP, high pericoronary adipose tissue attenuation and plaque progression, all of which are linked to MACE

[69]. These imaging modalities may be helpful in personalizing preventive strategies and optimizing CVD outcomes.

### 6.4. The future of cardiac CT: emerging technologies and their potential impact on preventive cardiology (Leandro Slipczuk, MD, PhD)

The ISCHEMIA trial noted that an initial invasive approach was not superior to conservative management in reducing the recurrence and total number of cardiovascular events in patients with stable CAD and moderate to severe ischemia [70]. This trial challenged the assumption that an invasive approach necessarily provides superior long-term benefits for stable CAD patients and highlighted the role of CCTA in diagnosis and management.

The advances in hardware development were underscored, highlighting photon-counting CT and spectral CT, allowing enhanced imaging quality with reduced radiation exposure and contrast dosage, boosting safety and effectiveness [71]. There has been an increased usage of routine chest CTs to identify CAC and thoracic aorta calcification (TAC), serving as early detection to allow prevention of cardiovascular events with pre-existing data [72]. Furthermore, the application of AI, deep learning, and machine learning in cardiac CT was highlighted as not only the future but also a current reality. However, the deployment of AI in research and clinical settings must be approached cautiously to prevent bias and ensure equitable healthcare outcomes across diverse populations of patients [73,74].

In addition, the concept of the CCTA-based radiomics signature for predicting coronary plaque behavior was explained. This approach holds the potential to tailor cardiology treatments basing the therapy on the specific patient phenotype [66]. New risk markers and special populations, such as young adults and patients with metabolic-associated steatosis liver disease (MASLD) or osteopenia, could potentially benefit from the use of cardiac CT in improving prognostic outcomes; for example, the identification of CAC and TAC in young patients with LDL  $\geq$ 190 mg/dL can help in risk stratification and management [75]. Selective use of CTA-guided prevention therapies may change the way we practice preventive medicine [76]; the importance of the SCOT-HEART 2 and TRANSFORM trials may provide new possibilities for CCTA, but cost-effectiveness analyses will be necessary [77].

## 7. Debates & emerging therapies

Debates featuring controversial issues in preventive cardiology have been a long-standing tradition of the ASPC (including in collaboration with the AHA) since its early years. The 2024 ASPC Congress featured debates on the therapeutic impact of colchicine on LDL-C, CAC vs CCTA in refining ASCVD risk prevention, and Lp(a) as an actionable lipid marker.

### 7.1. Reducing residual cvd risk: adding colchicine vs. aggressive lipid lowering (Daniel Soffer, MD vs. Michael Wilkinson, MD)

Both residual LDL-C levels and inflammation represent essential components of residual ASCVD risk. The impact of colchicine on LAP volume was reported by Vaidya et al. in 2018 [78]. Their observational study included 80 patients with recent ACS (< 1 month) receiving either 0.5 mg/day colchicine + optimal medical therapy (OMT) or OMT alone over 1 year and noted a significant reduction in LAP volume and high-sensitivity C-reactive protein (hsCRP) in the colchicine + OMT arm [78].

In a randomized, double-blind trial involving 5522 patients with chronic coronary disease, colchicine 0.5 mg daily significantly reduced the risk of MACE compared to placebo, with a hazard ratio of 0.69 (95% CI 0.57–0.83,  $p < 0.001$ ) [79]. The secondary endpoint (cardiovascular death, myocardial infarction, or stroke) was also reduced (HR 0.72). However, non-cardiovascular mortality was higher in the colchicine

group, highlighting potential trade-offs in its use for cardiovascular risk reduction. In another randomized, double-blind trial of 4745 patients treated with colchicine within 30 days of MI, low-dose colchicine (0.5 mg daily) significantly reduced the composite risk of cardiovascular events, including cardiovascular death, resuscitated cardiac arrest, myocardial infarction, stroke, or urgent revascularization (HR 0.77, 95 % CI 0.61–0.96,  $p = 0.02$ ) [80]. Colchicine offers the advantages of easy accessibility and safety. However, its role in preventive therapy is still highly underutilized in clinical practice.

Conversely, the arsenal for further LDL-C reduction has significantly expanded, with a 'lower is better' approach in secondary prevention gaining increasing support. Bempedoic acid has also recently gained popularity as a lipid-lowering therapy, mainly due to prior reports of a 21.7 % reduction in LDL-C, particularly in statin-intolerant patients as previously discussed [9]. In conclusion, there was consensus that both approaches are complementary and should be considered in managing high-risk individuals.

### 7.2. CAC/CCTA is the imaging modality of choice in refining ascvd risk in primary prevention (Matthew Budoff, MD, FASPC vs. Seamus Whelton, MD, MPH)

The MESA study has previously documented that a higher CAC increases the short and long-term risk of ASCVD. Zero CAC has been specifically noted to portend a favorable long-term prognosis, while CAC  $\geq 300$  AU or  $>75$ th percentile portends a higher CV risk, requiring more intensive preventive care [81,82]. CAC is less expensive, requires less training to analyze, and has less radiation risk with comparable risk prediction to CCTA. CCTA appears useful in certain patient groups such as younger patients ( $<45$ – $50$  years old), those with a significant history of family CVD, and in those in whom surveillance of non-calcified plaque is being monitored after lipid-lowering therapy, with this last concept currently exclusively within research.

The conclusion was that while CAC is currently recommended for asymptomatic individuals [83] while CCTA is not, emerging research suggests that CCTA may offer benefits in specific subgroups. Ongoing research will shed more light into the role of CCTA in asymptomatic patients within the next few years.

### 7.3. Lp(a) in primary prevention is actionable today (Vera Bittner, MD, MSPH vs. Roger Blumenthal, MD, FASPC)

AJPC recently published an article regarding Lp(a) diagnostic and treatment algorithms [84]. In one study across five academic health centers associated with the University of California, only 0.3 % of 5553, 654 patients had prior Lp(a) testing [85]. Importantly, there are racial differences in Lp(a) measurements as non-Hispanic Black individuals have higher odds of Lp(a)  $\geq 50$  mg/dL as compared with non-Hispanic White individuals [86]. Overall, these aforementioned studies have shown a benefit in prioritizing Lp(a) measurement for individuals with prevalent ASCVD, calcific aortic valve disease, family history of premature ASCVD and suboptimal response to high-intensity statin therapy. Barriers to universal Lp(a) measurement have been previously described to be lack of a universal assay, physician burden from increased testing, and lack of clear consensus for management of high Lp(a). Current practice has focused on traditional risk factor control but future data on this topic may support Lp(a) treatment as an important step in primary and secondary prevention.

## 8. Inflammation and CVD (Brittany Weber, MD and Michael Garshick, MD)

The session provided an in-depth exploration of the inflammatory pathways contributing to atherosclerotic plaque formation and the role of inflammatory markers in CAD. The findings underscored the significance of combining lipid-lowering and anti-inflammatory therapies to

address cardiovascular risks, especially in patients with autoimmune diseases. The session also emphasized the importance of multidisciplinary approaches, involving cardiology, rheumatology, and dermatology, to effectively manage cardiovascular risks in patients with autoimmune diseases.

### 8.1. From Inflammation to plaque formation: tracing the pathways to atherosclerosis (David Patrick, MD, PhD)

There are multiple inflammatory pathways leading to atherosclerotic plaque formation in CAD. The process begins with LDL being engulfed by macrophages, forming modified LDL, which recruit other inflammatory cells, including T-cells and dendritic cells [87]. This process contributes to the formation of foam cells and fatty streaks [87]. Additionally, nitric oxide (NO) plays a central role in regulating endothelial cell function. Still, traditional risk factors such as smoking, hypertension, hyperlipidemia, and T2DM can disrupt NO production, leading to inappropriate endothelial cell activation [87]. This triggers an inflammatory cascade and the activation of Transforming Growth Factor- $\beta$ , Platelet-Derived Growth Factors, Heparin-binding EGF-like growth factors, and Fibroblast Growth Factors, resulting in smooth muscle cell migration, proliferation, and plaque progression.

Moreover, multiple studies have examined the relationship between increasing quartiles of baseline hsCRP and LDL-C levels as predictors of cardiovascular deaths, MACE, and all-cause deaths [88]. It was found that hsCRP was a strong predictor of future cardiovascular events. In the AFCAPS/TexCAPS trial consisting of 6605 participants with elevated LDL-C and hsCRP, lovastatin therapy reduced the hsCRP level by 14.8 % ( $p < 0.001$ ) which was associated with a lower rates of coronary events (number needed to treat for five years to prevent 1 event, 47;  $p = 0.005$ ) [89].

A comparison conducted by Conrad et al. of 446,449 individuals with one or more autoimmune diseases and a 2102,830 individuals matched cohort, cardiovascular disease rates per 1000 person-years showed an increased risk across ages and sexes in the autoimmune cohort (HR 1.56, 95 % CI 1.52–1.59) [90]. The increased risk is secondary to traditional risk factors, heightened inflammation driven by cytokines, T-cell-mediated injury, neutrophils, and complement activation, which can directly activate endothelial cells and contribute to plaque progression [88].

These findings underscore the need for combined therapies, including effective lipid-lowering and possibly anti-inflammatory drugs, to reduce residual cardiovascular risk. For instance, in the CANTOS trial comprising of 4833 patients with stable coronary atherosclerosis disease, patients receiving canakinumab (a monoclonal antibody targeting interleukin-1 beta) who achieved IL-6 levels below the median showed a 32 % reduction in MACE, a 52 % decrease in cardiovascular mortality, and a 48 % reduction in all-cause mortality ( $p < 0.001$ ) [91].

### 8.2. Targeting inflammation in autoimmunity to reduce cardiovascular disease: ready for primetime? (Jon Giles, MD, MPH)

In a meta-analysis by Zubieta et al. consisting of 24 studies and 111,758 patients, rheumatoid arthritis (RA) was associated with a 50 % increased risk of cardiovascular mortality compared to matched non-RA controls (meta-standardized mortality ratio 1.50, 95 % CI 1.39–1.61) [92]. Patients with RA also have a higher burden of atherosclerotic plaques, as detected by CCTA [93–95]. These plaques tend to be more inflamed and prone to rupture [96]. RA contributes to this increased risk through both a higher prevalence of traditional CVD risk factors, such as smoking and hypertension, and RA-specific factors, including elevated levels of inflammation, cytokines, T cells, and monocytes [97–99].

Furthermore, a meta-analysis of 34 studies consisting of 456,734 by Roubille et al. showed that the use of methotrexate (MTX) was associated with a 28 % reduction in all CVD events across eight cohort studies (HR 0.72, 95 % CI 0.57–0.91), while TNF inhibitors were linked to a 30

% reduction in CVD events across 16 cohort studies (HR 0.70, 95 % CI 0.54–0.90) [99]. Similar findings were reported by Kang EH et al. and Giles JT et al. for abatacept, tocilizumab, and etanercept [97,100].

In the TARGET trial by Solomon et al., tumor necrosis factor inhibitors (TNFi) were compared with triple therapy (sulfasalazine, hydroxychloroquine, and TNFi) in 115 RA patients with an inadequate response to MTX (median age of 58 years, 71 % women) [101]. The trial showed an 8 % decrease in fluorodeoxyglucose uptake ( $p = 0.001$ ), a marker of vascular inflammation, in both the TNFi and triple therapy groups. Solomon et al. reported that individuals with lower multi-biomarker disease activity scores, which is composed of multiple inflammation biomarkers, experienced the greatest reduction in arterial radiotracer uptake [101].

However, there are multiple adverse effects of immunomodulators. The ORAL Surveillance Safety Trial conducted by Ytterberg SR et al. involved 1455 RA patients undergoing MTX treatment and compared the JAK inhibitor tofacitinib with TNFi and observed the occurrence of MACE [102]. Tofacitinib was not non-inferior to TNFi, indicating that the risk of MACE was higher in tofacitinib. However, there was a numerically lower incidence of MACE among those at the highest CVD risk who were treated with statin therapy at baseline and received tofacitinib, underscoring the cardioprotective role of statins in mitigating adverse effects of JAK inhibitors.

### 8.3. Practical Insights from cardio-inflammation clinics: lessons learned and future directions (Michael Garshick, MD)

Conrad et al. demonstrated that in a cohort of 2.5 million patients in the United Kingdom, the development of CVD was 15.3 % in the auto-immune population compared to 11 % in matched controls [90]. The risk of CVD increased with the number of autoimmune diseases present and was observed across a broad spectrum of autoimmune and organ-specific conditions. Diverse cardiovascular manifestations were noted, including arrhythmias such as atrial fibrillation and supraventricular arrhythmia, as well as myocarditis, pericarditis, endocarditis, and accelerated atherosclerosis [90].

Autoimmune diseases like systemic lupus erythematosus and RA adversely affect lipid profiles. In the KALIBRA study by Robertson et al., initiation of immunomodulatory medications of IL-6 inhibitors in 11 RA patients decreased the LDL catabolic rate to 0.27 pools/day compared to 0.53 pools/day in controls ( $p = 0.006$ ), leading to worsening dyslipidemia [103]. Additionally, in a meta-analysis of 66 RCTs enrolled 38,574 patients, Maqsood et al. showed that JAK inhibitors used in autoimmune diseases increased the risk of venous thromboembolism in clinical trials lasting 12 months or more (odds ratio (OR) 2.38, 95 % CI 1.24–4.57,  $p = 0.01$ ) [104]. The results for MACE were similar but did not reach statistical significance (OR 1.19, 95 % CI 0.86–1.64) [104].

Similarly, Ytterberg et al. found that tofacitinib, a JAK inhibitor, had adverse effects on lipid profiles and increased the risk of MACE [102]. Therefore, when initiating JAK inhibitors, a comprehensive cardiovascular risk evaluation, including history, cardiovascular risk score, Lp(a), and hsCRP, should be performed [105]. In patients with high cardiovascular risk, cardiologists should be involved in mitigating the risk through aggressive lipid-lowering therapy, antiplatelet agents, and subclinical CAD testing thought CAC [105].

Despite the relationship between autoimmune disease, inflammation, and CVD risk, a survey of 100 patients with psoriasis revealed that only 36 were recommended for CVD screening, and only 34 were informed by healthcare professionals about the association between psoriasis and increased CVD risk [106]. However, 84 patients indicated they would be more receptive to discussing CVD risk through a multidisciplinary approach [92]. This led Garshick and Berger et al. to propose multidisciplinary management involving rheumatology, dermatology, and cardiology for effective and comprehensive care of autoimmune diseases with a high risk of developing CVD [107].

## 9. Nutrition, exercise, and metabolism (Danielle Belardo, MD, FASPC, Dharmesh Patel, MD, FASPC)

The session provided valuable insights into the relationship between diet composition, processed foods, and obesity. It explored the ongoing debate over low carbohydrate versus low-fat diets, discussing how each impacts fat oxidation, insulin secretion, and energy expenditure. Additionally, it highlighted the dangers of consuming ultra-processed foods, which significantly increase caloric intake and contribute to weight gain. The session underscored the importance of a well-balanced diet, emphasizing the need for caution with processed foods while promoting healthier eating habits.

### 9.1. Carbs, Calories, and processed foods: insights into obesity and diet composition (Kevin Hall, MD)

There is ongoing debate over whether a low-carbohydrate or low-fat diet is more effective in promoting a healthier lifestyle. Hall et al. compared a reduced carbohydrate (RC) diet to a reduced fat (RF) diet in 19 men and women without T2DM and with a BMI of  $\geq 30$  kg/m<sup>2</sup> [108]. The RC diet led to decreased daily insulin secretion, which in turn reduced calorie deposition in fat cells, increased fat oxidation ( $p < 0.001$ ), and reduced energy expenditure ( $p = 0.099$ ) [108]. However, the RF diet resulted in greater cumulative body fat loss ( $p < 0.001$ ). Similarly, Hall and Guo et al. found that the RF diet increased energy expenditure and led to more significant body fat loss [108].

Additionally, when Hall et al. compared a baseline diet to a low-carbohydrate ketogenic diet in 17 men without T2DM and with a BMI of  $\geq 25$  kg/m<sup>2</sup>, the ketogenic diet led to a rapid and sustained decrease in insulin secretion, an increase in ketosis, and increased fat oxidation, though with no significant difference in energy expenditure [109]. The session also emphasized the varying effects of diet composition: a low-carbohydrate, high-fat diet caused a greater drop in postprandial insulin, whereas a high-carbohydrate, low-fat diet led to lower energy intake and more body fat loss [110]. Thus, the debate between RC and RF diets remains a significant topic.

Furthermore, there are multiple dangers of widely available processed foods. Ultra-processed foods were shown to increase energy intake significantly and lead to weight gain, primarily through increased body fat [111]. This underscores the importance of being cautious about consuming ultra-processed foods despite their convenience and availability.

### 9.2. Combating cardiovascular risks: nutritional interventions for lipids, hypertension, and diabetes (Robert Ostfeld, MD, ScM)

Multiple studies have reported that there is a widespread deficiency of a healthy diet within the population and underscored the critical role of a healthy lifestyle in improving lipid profiles, hypertension, and T2DM management. According to the National Health and Nutrition Examination Survey of 11,696 participants from 2011–2018, only 0.7 % followed an ideal healthy diet, which has the potential to prevent 42.4 % of CVD events [112].

The 2019 ACC/AHA Primary Prevention of Cardiovascular Disease Guideline recommends a diet rich in fruits, vegetables, legumes, nuts, seeds, plant proteins, and fatty fish as optimal for the prevention of ASCVD (Class I recommendation) [4]. Numerous studies have demonstrated the positive impact of cholesterol-lowering diets on lipid profiles. Jenkins et al. found that in 34 patients with hyperlipidemia, randomized to a very-low-saturated-fat diet (control diet), the same diet plus 20 mg lovastatin (statin diet), and a diet high in plant-based products (portfolio diet), LDL-C levels decreased by  $8.5 \pm 1.9$  %,  $33.3 \pm 1.9$  %, and  $29.6 \pm 1.3$  %, respectively, after four weeks [113]. Additionally, a 30-year follow-up by Glenn et al. on a plant-based portfolio diet in 73,924 women showed a reduced risk of total CVD (pooled HR, 0.92 [95 % CI, 0.89–0.95]), coronary heart disease (pooled HR 0.92, 95 % CI



0.88–0.95), and stroke (pooled HR 0.92, 95 % CI 0.87–0.96) [114].

Plant-based diets have also shown favorable effects on hypertension management. In the CARDIA study by Steffen et al., a 15-year follow-up of 4304 participants aged 18–30 years revealed that plant food intake was inversely related to the development of hypertension [115]. The relative hazards of elevated blood pressure for higher quintiles of plant food intake were 0.64 compared to 0.83 in the lowest quintile ( $p = 0.01$ ) [115]. Neal et al. demonstrated that in individuals over 60 years of age with hypertension, the rates of stroke, MACE, and all-cause mortality were lower with a salt substitute (75 % sodium chloride and 25 % potassium chloride) than with regular salt (100 % sodium chloride) [116].

The Adventist Health Study, comprising of 60,903 Adventist Church members in the US by Tonstad et al., found that a complete vegetarian diet had the lowest incidence of T2DM at 2.9 %, compared to lacto-ovo vegetarians, pes-co-vegetarians, semi-vegetarians, and non-vegetarians [117]. Moreover, Sullivan et al. showed that over a 22-year follow-up of 11,965 patients with ASCVD, higher plant-based diet index scores were associated with a lower risk of T2DM (quintile 5 vs 1 HR 0.89, 95 % CI 0.80–0.98,  $p = 0.01$ ) [118].

Multiple risk factors for ASCVD—including T2DM, hypertension, and hyperlipidemia—can all be mitigated by adopting a healthier diet rich in plant-based foods. This is in line with the 2021 European Society Guidelines, which advocate for a healthier diet to prevent adverse cardiovascular outcomes and ensure comprehensive care [119].

### 9.3. The fiber factor: dietary strategies in diabetes and obesity prevention (Nicola Guess, RD, PhD)

Fiber has a pivotal role in diet for weight management, T2DM control, and CVD risk reduction. Fiber aids in weight management by enhancing satiety, promoting energy balance by increasing calorie excretion through feces, and diluting energy by lowering the caloric density of food [120]. Prior studies have reinforced the importance of incorporating vegetables and fiber into the diet to reduce calorie intake and support weight loss [121]. Additionally, a study by Simpson HC et al. in 27 patients with T2DM, demonstrated that a high-fiber diet improved glycemic control compared to a low carbohydrate diet (mean postprandial glucose  $7.6 \pm 1.2$  vs  $9.0 \pm 1.9$ ,  $p < 0.001$ ), independent of weight loss [122]. The session concluded with innovative strategies to increase fiber intake, such as partially replacing meat with legumes, incorporating more soy and pea protein products, and trying new unique recipes such as legume-based pastas.

## 10. Conclusion

The 2024 ASPC conference presented innovative research and valuable insights into the evolving field of preventive cardiology, with a particular focus on lipid-lowering therapies, cardiovascular-kidney-metabolic health, and the integration of precision medicine. This year's discussions and studies highlighted the growing understanding of interconnected cardiovascular, kidney, and metabolic diseases, emphasizing early intervention and the use of innovative diagnostic and therapeutic strategies like GLP-1 RA and advanced imaging techniques. The findings presented not only reinforced the importance of addressing traditional cardiovascular risk factors but also underscored the critical role of emerging technologies and novel therapies in shaping the future of preventive cardiology. As the field advances, these insights promise to help optimize clinical outcomes through personalized but also accessible and equitable care, offering new hope for reducing the burden of cardiovascular disease.

### CRediT authorship contribution statement

**Akhil A. Chandra:** Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **Carlos Espiche:** Writing – review & editing, Writing – original draft, Project

administration, Conceptualization. **Maisha Maliha:** Writing – review & editing, Writing – original draft, Project administration. **Salim S Virani:** Writing – review & editing, Visualization, Supervision. **Roger S Blumenthal:** Writing – review & editing, Visualization, Validation, Supervision. **Fatima Rodriguez:** Writing – review & editing, Validation, Supervision. **Nathan D Wong:** Writing – review & editing, Visualization, Validation, Supervision, Conceptualization. **Martha Gulati:** Writing – review & editing, Visualization, Validation, Supervision. **Leandro Slipczuk:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Conceptualization. **Michael D Shapiro:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization.

### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Leandro Slipczuk reports a relationship with Amgen Inc that includes: funding grants. Leandro Slipczuk reports a relationship with Philips North America LLC that includes: funding grants. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### References

- [1] Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;350:1495–504.
- [2] Grundy SM, Cleeman JI, Merz CN, Brewer Jr HB, Clark LT, Hunninghake DB, Pasternak RC, Smith Jr SC, Stone NJ. Implications of recent clinical trials for the National cholesterol education program adult treatment panel III guidelines. *Circulation* 2004;110:227–39.
- [3] Hayward RA, Krumholz HM. Three reasons to abandon low-density lipoprotein targets: an open letter to the adult treatment panel iv of the national institutes of health. *Circ Cardiovasc Qual Outcomes* 2012;5:2–5.
- [4] Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith Jr SC, Virani SS, Williams Sr KA, Yeboah J, Ziaeian B. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the american college of cardiology/american heart association task force on clinical practice guidelines. *Circulation* 2019;140:e563–95.
- [5] Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, Darius H, Lewis BS, Ophuis TO, Jukema JW, De Ferrari GM, Ruzyllo W, De Lucca P, Im K, Bohula EA, Reist C, Wiviott SD, Tershakovec AM, Musliner TA, Braunwald E, Califf RM. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med* 2015;372:2387–97.
- [6] Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, Kuder JF, Wang H, Liu T, Wasserman SM, Sever PS, Pedersen TR. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017;376:1713–22.
- [7] Nissen SE, Nicholls SJ. Results of the GLAGOV trial. *Cleve Clin J Med* 2017;84:e1–5.
- [8] Schwartz GG, Gabriel Steg P, Bhatt DL, Bittner VA, Diaz R, Goodman SG, Jukema JW, Kim YU, Li QH, Manvelian G, Pordy R, Sourdille T, White HD, Szarek M. Committees OO and Investigators. clinical efficacy and safety of alirocumab after acute coronary syndrome according to achieved Level of low-density lipoprotein cholesterol: a propensity score-matched analysis of the odyssey outcomes trial. *Circulation* 2021;143:1109–22.
- [9] Nissen SE, Lincoff AM, Brennan D, Ray KK, Mason D, Kastelein JJP, Thompson PD, Libby P, Cho L, Plutzky J, Bays HE, Moriarty PM, Menon V, Grobbee DE, Louie MJ, Chen CF, Li N, Bloedon L, Robinson P, Horner M, Sasiela WJ, McCluskey J, Davey D, Fajardo-Campos P, Petrovic P, Fedacko J, Zmuda W, Lukyanov Y, Nicholls SJ. Bempedoic acid and cardiovascular outcomes in statin-intolerant patients. *N Engl J Med*. 2023;388:1353–64.
- [10] Ray KK, Landmesser U, Leiter LA, Kallend D, Dufour R, Karakas M, Hall T, Troquay RP, Turner T, Visseren FL, Wijngaard P, Wright RS, Kastelein JJ. Inclisiran in patients at high cardiovascular risk with elevated ldl cholesterol. *N Engl J Med* 2017;376:1430–40.
- [11] Ray KK, Wright RS, Kallend D, Koenig W, Leiter LA, Raal FJ, Bischof JA, Richardson T, Jaros M, Wijngaard PLJ, Kastelein JJP. Two phase 3 trials of inclisiran in patients with elevated LDL cholesterol. *N Engl J Med* 2020;382:1507–19.
- [12] Santos RD, Nasir K, Shapiro MD. A step forward for long-acting pcsk9 inhibition: improvements without a breakthrough. *J Am Coll Cardiol* 2024;84:2048–50.
- [13] Bugiardini R, Bairey Merz CN. Angina with "normal" coronary arteries: a changing philosophy. *Jama*. 2005;293:477–84.

- [14] Shaw LJ, Bugiardini R, Merz CN. Women and ischemic heart disease: evolving knowledge. *J Am Coll Cardiol* 2009;54:1561–75.
- [15] Merz CN, Kelsey SF, Pepine CJ, Reichel N, Reis SE, Rogers WJ, Sharaf BL, Sopko G. The Women's Ischemia Syndrome Evaluation (WISE) study: protocol design, methodology and feasibility report. *J Am Coll Cardiol* 1999;33:1453–61.
- [16] Handberg EM, Merz CNB, Cooper-Dehoff RM, Wei J, Conlon M, Lo MC, Boden W, Frayne SM, Villines T, Spertus JA, Weintraub W, O'Malley P, Chaitman B, Shaw LJ, Budoff M, Rogatko A, Pepine CJ. Rationale and design of the women's ischemia trial to reduce events in nonobstructive CAD (WARRIOR) trial. *Am Heart J* 2021;237:90–103.
- [17] Lincoff AM, Brown-Franden K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF, Lingvay I, Oral TK, Michelsen MM, Plutzky J, Tornøe CW, Ryan DH. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med*. 2023;389:2221–32.
- [18] Ndumele CE, Rangaswami J, Chow SL, Neeland IJ, Tuttle KR, Khan SS, Coresh J, Mathew RO, Baker-Smith CM, Carnethon MR, Despres JP, Ho JE, Joseph JJ, Kernan WN, Khera A, Kosiborod MN, Lekavich CL, Lewis EF, Lo KB, Ozkan B, Palaniappan LP, Patel SS, Pencina MJ, Powell-Wiley TM, Sperling LS, Virani SS, Wright JT, Rajgopal Singh R, Elkind MSV. Cardiovascular-kidney-metabolic health: a presidential advisory from the American Heart Association. *Circulation* 2023;148:1606–35.
- [19] Budoff MJ, Kinninger A, Gransar H, Achenbach S, Al-Mallah M, Bax JJ, Berman DS, Cademartiri F, Callister TQ, Chang HJ, Chow BJW, Cury RC, Feuchtnr G, Hadamitzky M, Hausleiter J, Kaufmann PA, Leipsic J, Lin FY, Kim YJ, Marques H, Pontone G, Rubinshtein R, Shaw LJ, Villines TC, JK Min. When does a calcium score equate to secondary prevention?: insights from the multinational confirm registry. *JACC Cardiovasc Imaging* 2023;16:1181–9.
- [20] Reyes-Soffer G, Yeang C, Michos ED, Boatwright W, Ballantyne CM. High lipoprotein(a): actionable strategies for risk assessment and mitigation. *Am J Prev Cardiol* 2024;18:100651.
- [21] Rivera FB, Cha SW, Varona MC, Fernandez Co EM, Magalong JV, Aparece JP, De Oliveira-Gomes D, Kaur G, Gulati M. Atherosclerotic coronary plaque regression from lipid-lowering therapies: a meta-analysis and meta-regression. *Am J Prev Cardiol* 2024;18:100645.
- [22] Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, Liu K, Shea S, Szklo M, Bluemke DA, O'Leary DH, Tracy R, Watson K, Wong ND, Kronmal RA. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 2008;358:1336–45.
- [23] Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, Foster E, Hlatky MA, Hodgson JM, Kushner FG, Lauer MS, Shaw LJ, Smith Jr SC, Taylor AJ, Weintraub WS, Wenger NK, Jacobs AK. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: executive summary: a report of the American college of cardiology foundation/American heart association task force on practice guidelines. *Circulation* 2010;122:2748–64.
- [24] Fernández-Ortiz A, Jiménez-Borreguero LJ, Peñalvo JL, Ordovás JM, Mocoroa A, Fernández-Friera L, Laclaustra M, García L, Molina J, Mendiguren JM, López-Melgar B, de Vega VM, Alonso-Farto JC, Guallar E, Sillesen H, Rudd JH, Fayad ZA, Ibañez B, Sanz G, Fuster V. The Progression and Early detection of subclinical atherosclerosis (PESA) study: rationale and design. *Am Heart J* 2013;166:990–8.
- [25] Ibañez B, Fernández-Ortiz A, Fernández-Friera L, García-Lunar I, Andrés V, Fuster V. Progression of early subclinical atherosclerosis (PESA) Study. *J Am Coll Cardiol* 2021;78:156–79.
- [26] Fernández-Friera L, Peñalvo JL, Fernández-Ortiz A, Ibañez B, López-Melgar B, Laclaustra M, Oliva B, Mocoroa A, Mendiguren J, V Martínez de Vega, García L, Molina J, Sánchez-González J, Guzmán G, Alonso-Farto JC, Guallar E, Civeira F, Sillesen H, Pocock S, Ordovás JM, Sanz G, Jiménez-Borreguero LJ, Prevalence Fuster V. Vascular distribution, and multiterritorial extent of subclinical atherosclerosis in a middle-aged cohort: the pesa (progression of early subclinical atherosclerosis) study. *Circulation* 2015;131:2104–13.
- [27] Lloyd-Jones Donald M, Lewis Cora E, Schreiner Pamela J, Shikany James M, Sidney S, Reis Jared P. The coronary artery risk development in young adults (CARDIA) Study. *J Am Coll Cardiol* 2021;78:260–77.
- [28] Bibbins-Domingo K, Pletcher MJ, Lin F, Vittinghoff E, Gardin JM, Arynchyn A, Lewis CE, Williams OD, Hulley SB. Racial differences in incident heart failure among young adults. *N Engl J Med* 2009;360:1179–90.
- [29] Shah NS, Ning H, Petito LC, Kershaw KN, Bancks MP, Reis JP, Rana JS, Sidney S, Jacobs DR, Kiefe CI, Carnethon MR, Lloyd-Jones DM, Allen NB, Khan SS. Associations of clinical and social risk factors with racial differences in premature cardiovascular disease. *Circulation* 2022;146:201–10.
- [30] Bancks MP, Kershaw K, Carson AP, Gordon-Larsen P, Schreiner PJ, Carnethon MR. Association of modifiable risk factors in young adulthood with racial disparity in incident type 2 diabetes during middle adulthood. *JAMA* 2017;318:2457–65.
- [31] Gunderson EP, Sun B, Catov JM, Carnethon M, Lewis CE, Allen NB, Sidney S, Wellons M, Rana JS, Hou L, Carr JJ. Gestational diabetes history and glucose tolerance after pregnancy associated with coronary artery calcium in women during midlife: the cardia study. *Circulation* 2021;143:974–87.
- [32] Seo Y, Moon J, Lee H-H, Kim HC, Kaneko F, Shin S, Kim E, Bae J-W, Kim B-K, Lee S-J, Kim M, Lee H. Incidence and case fatality of acute myocardial infarction in Korea, 2011–2020. *Epidemiol Health* 2023:e2024002.
- [33] Lee H, Yano Y, Lloyd-Jones DM and Kim HC. Adherence to antihypertensive medication and incident cardiovascular events in young adults with hypertension. 2021.
- [34] Blazing MA, Giugliano RP, Cannon CP, Musliner TA, Tereshakovec AM, White JA, Reist C, McCagg A, Braunwald E, Califf RM. Evaluating cardiovascular event reduction with ezetimibe as an adjunct to simvastatin in 18,144 patients after acute coronary syndromes: Final baseline characteristics of the IMPROVE-IT study population. *Am Heart J* 2014;168:205–12. e1.
- [35] Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, Braun LT, de Ferranti S, Faiella-Tommasino J, Forman DE, Goldberg R, Heidenreich PA, Hlatky MA, Jones DW, Lloyd-Jones D, Lopez-Pajares N, Ndumele CE, Orringer CE, Peralta CA, Saseen JJ, Smith Jr SC, Sperling L, Virani SS, Yeboah J. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. *J Am Coll Cardiol* 2019;73:3168–209.
- [36] Bruckert E, Hayem G, Dejager S, Yau C, Bégaud B. Mild to moderate muscular symptoms with high-dosage statin therapy in hyperlipidemic patients—the PRIMO Study. *Cardiovasc Drugs Ther* 2005;19:403–14.
- [37] Dormuth CR, Filion KB, Paterson JM, James MT, Teare GF, Raymond CB, Rahme E, Tamim H. Lipscombe L and for the Canadian Network for Observational Drug Effect Studies I. Higher potency statins and the risk of new diabetes: multicentre, observational study of administrative databases. *BMJ* 2014;348:g3244. -g3244.
- [38] Shin J-I, Fine DM, Sang Y, Surapaneni A, Dunning SC, Inker LA, Nolin TD, Chang AR, Grams ME. Association of rosuvastatin use with risk of hematuria and Proteinuria. *JASN* 2022;33:1767–77.
- [39] Giugliano RP, Wiviott SD, Blazing MA, De Ferrari GM, Park J-G, Murphy SA, White JA, Tereshakovec AM, Cannon CP, Braunwald E. Long-term safety and efficacy of achieving very low levels of low-density lipoprotein cholesterol: a prespecified analysis of the improve-it Trial. *JAMA Cardiol* 2017;2:547.
- [40] Kim B-K, Hong S-J, Lee Y-J, Hong SJ, Yun KH, Hong B-K, Heo JH, Rha S-W, Cho Y-H, Lee S-J, Ahn C-M, Kim J-S, Ko Y-G, Choi D, Jang Y, Hong M-K. Long-term efficacy and safety of moderate-intensity statin with ezetimibe combination therapy versus high-intensity statin monotherapy in patients with atherosclerotic cardiovascular disease (RACING): a randomised, open-label, non-inferiority trial. *The Lancet* 2022;400:380–90.
- [41] Leopold JA, Loscalzo J. Emerging role of precision medicine in cardiovascular disease. *Circ Res* 2018;122:1302–15.
- [42] Reza N, Alford RL, Belmont JW, Marston N. The expansion of genetic testing in cardiovascular medicine: preparing the cardiology community for the changing landscape. *Curr Cardiol Rep* 2024;26:135–46.
- [43] Patel AP, Wang M, Ruan Y, Koyama S, Clarke SL, Yang X, Tcheandjieu C, Agrawal S, Fahed AC, Ellinor PT, Genes Health, Research T, Million Veteran P, Tsao PS, Sun YV, Cho K, Wilson PWF, Assimes TL, Van Heel DA, Butterworth AS, Aragam KG, Natarajan P, Khera AV. A multi-ancestry polygenic risk score improves risk prediction for coronary artery disease. *Nat Med* 2023;29:1793–803.
- [44] Natarajan P. Genomic aging, clonal hematopoiesis, and cardiovascular disease. *ATVB* 2023;43:3–14.
- [45] Lennon NJ, Kottyan LC, Kachulis C, Abul-Husn NS, Arias J, Belbin G, Below JE, Berndt SI, Chung WK, Cimino JJ, Clayton EW, Connolly JJ, Crosslin DR, Dikilitas O, Velez Edwards DR, Feng Q, Fisher M, Freimuth RR, Ge T, The GC, Berndt S, Hirschhorn J, Loos R, The All of US Research P, Glessner JT, Gordon AS, Patterson C, Hakonarson H, Harden M, Harr M, Hirschhorn JN, Hoggart C, Hsu L, Irvin MR, Jarvik GP, Karlson EW, Khan A, Khera A, Kiryluk K, Kullo I, Larkin K, Limdi N, Linder JE, Loos RJF, Luo Y, Malolepsza E, Manolio TA, Martin LJ, McCarthy L, McNally EM, Meigs JB, Mersha TB, Mosley JD, Musick A, Namjou B, Pai N, Pesce LL, Peters U, Peterson JF, Prows CA, Puckelwartz MJ, Rehm HL, Roden DM, Rosenthal EA, Rowley R, Sawicki KT, Schaid DJ, Smit RAJ, Smith JL, Smoller JW, Thomas M, Tiwari H, Toledo DM, Vaitadin NS, Veenstra D, Walunas TL, Wang Z, Wei W-Q, Weng C, Wiesner GL, Yin X, Kenny EE. Selection, optimization and validation of ten chronic disease polygenic risk scores for clinical implementation in diverse US populations. *Nat Med* 2024;30:480–7.
- [46] Helgason H, Eiriksdottir T, Ulfarsson MO, Choudhary A, Lund SH, Ivarsdottir EV, Hjorleifsson Eldjarn G, Einarsson G, Ferkingstad E, Moore KHS, Honarpour N, Liu T, Wang H, Hucko T, Sabatine MS, Morrow DA, Giugliano RP, Ostrowski SR, Pedersen OB, Bundgaard H, Erikstrup C, Arnar DO, Thorgerisson G, Masson G, Magnusson OT, Saemundsdottir J, Gretarsdottir S, Steinthorsdottir V, Thorleifsson G, Helgadóttir A, Sulem P, Thorsteinsdottir U, Holm H, Gudbjartsson D, Stefansson K. Evaluation of large-scale proteomics for prediction of cardiovascular events. *JAMA* 2023;330:725.
- [47] Schuermans A, Honigberg MC, Raffield LM, Yu B, Roberts MB, Kooperberg C, Desai P, Carson AP, Shah AM, Ballantyne CM, Bick AG, Natarajan P, Manson JE, Whitsel EA, Eaton CB, Reiner AP. Clonal hematopoiesis and incident heart failure with preserved ejection fraction. *JAMA Netw Open* 2024;7:e2353244.
- [48] Weiss J, Raghu VK, Paruchuri K, Zinzuwadia A, Natarajan P, Aerts HJWL, Lu MT. Deep learning to estimate cardiovascular risk from chest radiographs: a risk prediction study. *Ann Intern Med* 2024;177:409–17.
- [49] Wing RR, Bolin P, Brancati FL, Bray GA, Clark JM, Coday M, Crow RS, Curtis JM, Egan CM, Espeland MA, Evans M, Foreyt JP, Ghazarian S, Gregg EW, Harrison B, Hazuda HP, Hill JO, Horton ES, Hubbard VS, Jakicic JM, Jeffery RW, Johnson KC, Kahn SE, Kitabchi AE, Knowler WC, Lewis CE, Maschak-Carey BJ, Montez MG, Murrillo A, Nathan DM, Patricio J, Peters A, Pi-Sunyer X, Pownall H, Reboussin D, Regensteiner JG, Rickman AD, Ryan DH, Safford M, Wadden TA, Wagenknecht LE, West DS, Williamson DF, Yanovski SZ. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013;369:145–54.
- [50] Kosiborod MN, Abildstrøm SZ, Borlaug BA, Butler J, Rasmussen S, Davies M, Hovingh GK, Kitzman DW, Lindgaard ML, Møller DV, Shah SJ, Treppendahl MB, Verma S, Abhayaratna W, Ahmed FZ, Chopra V, Ezekowitz J, Fu M, Ito H, Lelonek M, Melenovsky V, Merkely B, Núñez J, Perna E, Schou M, Senni M,

- Sharma K, Van der Meer P, von Lewinski D, Wolf D, Petrie MC. Semaglutide in patients with heart failure with preserved ejection fraction and obesity. *N Engl J Med* 2023;389:1069–84.
- [51] Ussher JR, Drucker DJ. Glucagon-like peptide 1 receptor agonists: cardiovascular benefits and mechanisms of action. *Nat Rev Cardiol* 2023;20:463–74.
- [52] Drucker DJ. The GLP-1 journey: from discovery science to therapeutic impact. *J Clin Invest* 2024;134:e175634.
- [53] Chuang MH, Chen JY, Wang HY, Jiang ZH, Wu VC. Clinical outcomes of tirzepatide or glp-1 receptor agonists in individuals with type 2 diabetes. *JAMA Netw Open* 2024;7:e2427258.
- [54] Nicholls SJ, Bhatt DL, Buse JB, Prato SD, Kahn SE, Lincoff AM, McGuire DK, Nauck MA, Nissen SE, Sattar N, Zimman B, Zoungas S, Basile J, Barteo A, Miller D, Nishiyama H, Pavo I, Weerakkody G, Wiese RJ, D'Alessio D. Comparison of tirzepatide and dulaglutide on major adverse cardiovascular events in participants with type 2 diabetes and atherosclerotic cardiovascular disease: SURPASS-CVOT design and baseline characteristics. *Am Heart J* 2024;267:1–11.
- [55] Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, Kiyosue A, Zhang S, Liu B, Bunck MC, Stefanski A. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med* 2022;387:205–16.
- [56] Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JF, Nauck MA, Nissen SE, Pocock S, Poulter NR, Ravn LS, Steinberg WM, Stockner M, Zimman B, Bergenstal RM, Buse JB. Liraglutide and Cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2016;375:311–22.
- [57] Marso SP, Bain SC, Consoi A, Eliaschewitz FG, Jódar E, Leiter LA, Lingvay I, Rosenstock J, Seufert J, Warren ML, Woo V, Hansen O, Holst AG, Pettersson J, Vilsbøll T. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2016;375:1834–44.
- [58] Aroda VR, Rosenstock J, Terauchi Y, Altuntas Y, Lalic NM, Morales Villegas EC, Jeppesen OK, Christiansen E, Hertz CL, Haluzik M. PIONEER 1: randomized clinical trial of the efficacy and safety of oral semaglutide monotherapy in comparison with placebo in patients with type 2 diabetes. *Diabetes Care* 2019;42:1724–32.
- [59] Husain M, Birkenfeld AL, Donsmark M, Dungan K, Eliaschewitz FG, Franco DR, Jeppesen OK, Lingvay I, Mosenzon O, Pedersen SD, Tack CJ, Thomsen M, Vilsbøll T, Warren ML, Bain SC. Oral semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2019;381:841–51.
- [60] Khan SS, Ning H, Wilkins JT, Allen N, Carnethon M, Berry JD, Sweis RN, Lloyd-Jones DM. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. *JAMA Cardiol* 2018;3:280.
- [61] Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, Blankstein R, Boyd J, Bullock-Palmer RP, Conejo T, Diercks DB, Gentile F, Greenwood JP, Hess EP, Hollenber SM, Jaber WA, Jneid H, Joglar JA, Morrow DA, O'Connor RE, Ross MA, Shaw LJ. 2021 AHA/ACC/AASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: a report of the American college of cardiology/American heart association joint committee on clinical practice guidelines. *Circulation*. 2021;144:e368–454.
- [62] Knuuti J, Ballo H, Juarez-Orozco LE, Saraste A, Kolh P, Rutjes AWS, Jüni P, Windecker S, Bax JJ, Wijns W. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. *Eur Heart J* 2018;39:3322–30.
- [63] Hoffmann U, Ferencik M, Udelson JE, Picard MH, Truong QA, Patel MR, Huang M, Pencina M, Mark DB, Heitner JF, Fordyce CB, Pellikka PA, Tardif J-C, Budoff M, Nahhas G, Chow B, Kosinski AS, Lee KL, Douglas PS, Investigators P. Prognostic value of noninvasive cardiovascular testing in patients with stable chest pain: insights from the promise trial (prospective multicenter imaging study for evaluation of chest pain). *Circulation* 2017;135:2320–32.
- [64] van Rosendaal AR, Lin FY, van den Hoogen IJ, Ma X, Gianni U, Al Hussein Alawamlh O, Al'Aref SJ, Peña JM, Andreini D, Budoff MJ, Cademartiri F, Chinnaiyan K, Choi JH, Conte E, Marques H, de Araújo Gonçalves P, Gottlieb I, Hadamitzky M, Leipsic J, Maffei E, Pontone G, Raff GL, Shin S, Kim Y-J, Lee BK, Chun EJ, Sung JM, Lee S-E, Han D, Berman DS, Virmani R, Samady H, Stone P, Narula J, Bax JJ, Shaw LJ, Min JK, Chang H-J. Progression of whole-heart atherosclerosis by coronary ct and major adverse cardiovascular events. *J Cardiovasc Comput Tomogr* 2021;15:322–30.
- [65] Williams MC, Kwiecinski J, Doris M, McElhinney P, D'Souza MS, Cadet S, Adamson PD, Moss AJ, Alam S, Hunter A, Shah ASV, Mills NL, Pawade T, Wang C, Weir McCall J, Bonnici-Mallia M, Murrills C, Roditi G, van Beek EJR, Shaw LJ, Nicol ED, Berman DS, Slomka PJ, Newby DE, Dweck MR, Dey D. Low-attenuation noncalcified plaque on coronary computed tomography angiography predicts myocardial infarction: results from the multicenter scot-heart trial (scottish computed tomography of the heart). *Circulation* 2020;141:1452–62.
- [66] Lin A, Dey D. CT-based radiomics and machine learning for the prediction of myocardial ischemia: toward increasing quantification. *J Nucl Cardiol* 2022;29:275–7.
- [67] Lin A, Manral N, McElhinney P, Killekar A, Matsumoto H, Kwiecinski J, Pieszko K, Razipour A, Grodecki K, Park C, Otaki Y, Doris M, Kwan AC, Han D, Kuronuma K, Flores Tomasino G, Tzolos E, Shanbhag A, Goeller M, Marwan M, Gransar H, Tamarappoo BK, Cadet S, Achenbach S, Nicholls SJ, Wong DT, Berman DS, Dweck M, Newby DE, Williams MC, Slomka PJ, Dey D. Deep learning-enabled coronary CT angiography for plaque and stenosis quantification and cardiac risk prediction: an international multicenter study. *Lancet Digit Health* 2022;4:e256–65.
- [68] Shiyovich A, Berman AN, Besser SA, Biery DW, Cardoso R, Divakaran S, Singh A, Huck DM, Weber B, Plutzky J, Cannon C, Nasir K, Di Carli MF, Januzzi JL, Bhatt DL, Blankstein R. Lipoprotein(a) as a cardiovascular risk factor among patients with and without diabetes Mellitus: the Mass General Brigham Lp(a) Registry. *Cardiovasc Diabetol* 2024;23:257.
- [69] Nurmohamed NS, Gaillard EL, Malkasian S, de Groot RJ, Ibrahim S, Bom MJ, Kaiser Y, Earls JP, Min JK, Kroon J, Planken RN, Danan I, van Rosendaal AR, Choi AD, Stroes ESG and Knaapen P. Lipoprotein(a) and Long-term plaque progression, low-density plaque, and pericoronary inflammation. 2024.
- [70] Lopez-Sendon JL, Cyr DD, Mark DB, Bangalore S, Huang Z, White HD, Alexander KP, Li J, Nair RG, Demkow M, Peteiro J, Wander GS, Demchenko EA, Gamma R, Gadkari M, Poh KK, Nageh T, Stone PH, Keltai M, Sidhu M, Newman JD, Boden WE, Reynolds HR, Chaitman BR, Hochman JS, Maron DJ, O'Brien SM. Effects of initial invasive vs. initial conservative treatment strategies on recurrent and total cardiovascular events in the ISCHEMIA trial. *Eur Heart J* 2022;43:148–9.
- [71] Simon J, Á Hrenkó, Kerkovits NM, Nagy K, Vértes M, Balogh H, Nagy N, Munkácsi T, Emrich T, Varga-Szemes A, Boussoussou M, Vattay B, Vecsey-Nagy M, Kolossváry M, Szilveszter B, Merkely B, Maurovich-Horvat P. Photon-counting detector CT reduces the rate of referrals to invasive coronary angiography as compared to CT with whole heart coverage energy-integrating detector. *J Cardiovasc Comput Tomogr* 2024;18:69–74.
- [72] Castagna F, Miles J, Arce J, Leiderman E, Neshiwat P, Ippolito P, Friedmann P, Schenone A, Zhang L, Rodriguez CJ, Blaha MJ, Levsky JM, Garcia MJ, Slipczuk L. Visual coronary and aortic calcium scoring on chest computed tomography predict mortality in patients with low-density lipoprotein-cholesterol  $\geq 190$  mg/dL. *Circ Cardiovasc Imaging* 2022:15.
- [73] Tzolos E, Williams MC, McElhinney P, Lin A, Grodecki K, Flores Tomasino G, Cadet S, Kwiecinski J, Doris M, Adamson PD, Moss AJ, Alam S, Hunter A, Shah ASV, Mills NL, Pawade T, Wang C, Weir-McCall JR, Roditi G, van Beek EJR, Shaw LJ, Nicol ED, Berman DS, Slomka PJ, Dweck MR, Newby DE, Dey D. Pericoronary Adipose tissue attenuation, low-attenuation plaque burden, and 5-year risk of myocardial infarction. *JACC Cardiovasc Imaging* 2022;15:1078–88.
- [74] Obermeyer Z, Powers B, Vogeli C, Mullainathan S. Dissecting racial bias in an algorithm used to manage the health of populations. *Science* 2019;366:447–53.
- [75] Ahmadi N, Mao SS, Hajsadeghi F, Arnold B, Kiramijyan S, Gao Y, Flores F, Azen S, Budoff M. The relation of low levels of bone mineral density with coronary artery calcium and mortality. *Osteoporos Int* 2018;29:1609–16.
- [76] Apple SJ, Clark R, Daich J, Gonzalez ML, Ostfeld RJ, Toth PP, Bittner V, Martin SS, Rana JS, Nasir K, Shapiro MD, Virani SS, Slipczuk L. Closing the gaps in care of dyslipidemia: revolutionizing management with digital health and innovative care models. *Rev Cardiovasc Med* 2023;24:350.
- [77] McDermott M, Meah MN, Khaing P, Wang K-L, Ramsay J, Scott G, Rickman H, Burt T, McGowan I, Fairbairn T, Bucukoglu M, Bull R, Timmis A, Van Beek EJR, Roditi G, Adamson PD, Lewis S, Norrie J, McKinstry B, Guthrie B, Ritchie L, Mills NL, Dweck MR, Williams MC, Newby DE. Rationale and design of SCOT-HEART 2 Trial. *JACC Cardiovasc Imaging* 2024;19:36878X24002286.
- [78] Vaidya K, Arnott C, Martínez GJ, Ng B, McCormack S, Sullivan DR, Celermajor DS, Patel S. Colchicine Therapy and plaque stabilization in patients with acute coronary syndrome: a CT coronary angiography study. *JACC Cardiovasc Imaging* 2018;11:305–16.
- [79] Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TJSJ, The SHK, Xu XF, Ireland MA, Lenderink T, Latchem D, Hoogslag P, Jerzowski A, Nierop P, Whelan A, Hendriks R, Swart H, Schaap J, Kuijper AFM, van Hensen MWJ, Saklani P, Tan I, Thompson AG, Morton A, Judkins C, Bax WA, Dirksen M, Alings M, Hankey GJ, Budgeon CA, Tijssen JGP, Cornel JH, Thompson PL. Colchicine in patients with chronic coronary disease. *N Engl J Med* 2020;383:1838–47.
- [80] Tardif JC, Kouz S, Waters DD, Bertrand OF, Diaz R, Maggioni AP, Pinto FJ, Ibrahim R, Gama H, Kiwan GS, Berry C, López-Sendón J, Ostadal P, Koenig W, Angoulvant D, Grégoire JC, Lavoie MA, Dubé MP, Rhoads D, Provencher M, Blondeau L, Orfanos A, L'Allier PL, Guertin MC, Roubille F. Efficacy and safety of low-dose colchicine after myocardial infarction. *N Engl J Med* 2019;381:2497–505.
- [81] Dzybe O, Dardari ZA, Cainzos-Achirica M, Blankstein R, Agatston AS, Duebgen M, Yeboah J, Szklo M, Budoff MJ, Lima JAC, Blumenthal RS, Nasir K, Blaha MJ. Warranty period of a calcium score of zero: comprehensive analysis from MESA. *JACC Cardiovasc Imaging* 2021;14:990–1002.
- [82] Hadamitzky M, Achenbach S, Al-Mallah M, Berman D, Budoff M, Cademartiri F, Callister T, Chang HJ, Cheng V, Chinnaiyan K, Chow BJ, Cury R, Delago A, Dunning A, Feuchtnner G, Gomez M, Kaufmann P, Kim YJ, Leipsic J, Lin FY, Maffei E, Min JK, Raff G, Shaw LJ, Villines TC, Hausleiter J. Optimized prognostic score for coronary computed tomographic angiography: results from the CONFIRM registry (COronary CT Angiography Evaluation For Clinical Outcomes: an international Multicenter Registry). *J Am Coll Cardiol* 2013;62:468–76.
- [83] Piña P, Lorenzatti D, Paula R, Daich J, Schenone AL, Gongora C, Garcia MJ, Blaha MJ, Budoff MJ, Berman DS, Virani SS, Slipczuk L. Imaging subclinical coronary atherosclerosis to guide lipid management, are we there yet? *Am J Prev Cardiol* 2023;13:100451.
- [84] Razavi AC. Precise versus pragmatic - a perspective and evaluation of Lipoprotein(a) testing recommendations: A fellow's voice. *Am J Prev Cardiol* 2024;17:100637.
- [85] Bhatia HS, Hurst S, Desai P, Zhu W, Yeang C. Lipoprotein(a) testing trends in a large academic health system in the United States. *J Am Heart Assoc* 2023;12:e031255.
- [86] Dudum R, Huang Q, Yan X, Fonseca Marina A, Jose P, Sarraju A, Palaniappan L, Rodriguez F. Lipoprotein(a) Levels in disaggregated racial and ethnic subgroups across atherosclerotic cardiovascular disease risk levels. *JACC Advances* 2024;3:100940.

- [87] Linton MF, Yancey PG, Davies SS, Jerome WG, Linton EF, Song WL, Doran AC, Vickers KC. The Role of Lipids and Lipoproteins in Atherosclerosis. eds. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, de Herder WW, Dhatariya K, Dungan K, Hofland J, Kalra S, Kaltsas G, Kapoor N, Koch C, Kopp P, Korbonits M, Kovacs CS, Kuohung W, Laferrère B, Levy M, McGee EA, McLachlan R, New M, Purnell J, Sahay R, Shah AS, Singer F, Sperling MA, Stratakis CA, Trencle DL, Wilson DP, editors. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; 2000. Copyright © 2000-2024.
- [88] Fonseca FAH, MC Izar. Inflammation in Cardiovascular disease: current status and future perspectives. *Inte J Cardiovasc Sci* 2023;36: -.
- [89] Downs JR, Clearfield M, Weis S, Whitney E, Shapiro DR, Beere PA, Langendorfer A, Stein EA, Krueger W, Gotto Jr AM. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. *Air Force/Texas Coronary Atherosclerosis Prevention Study*. *JAMA* 1998;279:1615–22.
- [90] Conrad N, Verbeke G, Molenberghs G, Goetschalckx L, Callender T, Cambridge G, Mason JC, Rahimi K, McMurray JVV, Verbeke JY. Autoimmune diseases and cardiovascular risk: a population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK. *Lancet* 2002;400:733–43.
- [91] Ridker PM, Libby P, MacFadyen JG, Thuren T, Ballantyne C, Fonseca F, Koenig W, Shimokawa H, Everett BM, Glynn RJ. Modulation of the interleukin-6 signalling pathway and incidence rates of atherosclerotic events and all-cause mortality: analyses from the Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS). *Eur Heart J* 2018;39:3499–507.
- [92] Aviña-Zubieta JA, Choi HK, Sadatsafavi M, Etmann M, Esdaile JM, Lacaille D. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. *Arthritis Rheum* 2008;59:1690–7.
- [93] Chung CP, Giles JT, Petri M, Szklo M, Post W, Blumenthal RS, Gelber AC, Ouyang P, Jenny NS, Bathon JM. Prevalence of traditional modifiable cardiovascular risk factors in patients with rheumatoid arthritis: comparison with control subjects from the multi-ethnic study of atherosclerosis. *Semin Arthritis Rheum* 2012;41:535–44.
- [94] Chung CP, Oeser A, Raggi P, Gebretsadik T, Shintani AK, Sokka T, Pincus T, Avalos I, Stein CM. Increased coronary-artery atherosclerosis in rheumatoid arthritis: relationship to disease duration and cardiovascular risk factors. *Arthritis Rheum* 2005;52:3045–53.
- [95] Karpouzas GA, Malpeso J, Choi T-Y, Li D, Munoz S, Budoff MJ. Prevalence, extent and composition of coronary plaque in patients with rheumatoid arthritis without symptoms or prior diagnosis of coronary artery disease. *Ann Rheum Dis* 2014;73:1797–804.
- [96] Aubry M-C, Maradit-Kremers H, Reinalda MS, Crowson CS, Edwards WD, Gabriel SE. Differences in atherosclerotic coronary heart disease between subjects with and without rheumatoid arthritis. *J Rheumatol* 2007;34:937–42.
- [97] Giles JT, Sattar N, Gabriel S, Ridker PM, Gay S, Warne C, Musselman D, Brockwell L, Shittu E, Klearman M, Fleming TR. Cardiovascular safety of tocilizumab versus etanercept in rheumatoid arthritis: a randomized controlled trial. *Arthritis Rheumatol* 2020;72:31–40.
- [98] Nissen SE, Yeomans ND, Solomon DH, Lüscher TF, Libby P, Husni ME, Graham DY, Borer JS, Wisniewski LM, Wolksi KE, Wang Q, Menon V, Ruschitzka F, Gaffney M, Beckerman B, Berger MF, Bao W, Lincoff AM. Cardiovascular Safety of celecoxib, naproxen, or ibuprofen for arthritis. *N Engl J Med* 2016;375:2519–29.
- [99] Roubille C, Richer V, Starnino T, McCourt C, McFarlane A, Fleming P, Siu S, Kraft J, Lynde C, Pope J, Gulliver W, Keeling S, Dutz J, Bessette L, Bissonnette R, Haraoui B. The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis. *Ann Rheum Dis* 2015;74:480–9.
- [100] Kang EH, Jin Y, Brill G, Lewey J, Patorno E, Desai RJ, Kim SC. Comparative cardiovascular risk of abatacept and tumor necrosis factor inhibitors in patients with rheumatoid arthritis with and without diabetes mellitus: a multidatabase cohort study. *J Am Heart Assoc* 2018;7.
- [101] Solomon DH, Giles JT, Liao KP, Ridker PM, Rist PM, Glynn RJ, Broderick R, Lu F, Murray MT, Vanni K, Santacroce LM, Abohashem S, Robson PM, Fayad Z, Mani V, Tawakol A, Bathon J. Reducing cardiovascular risk with immunomodulators: a randomised active comparator trial among patients with rheumatoid arthritis. *Ann Rheum Dis* 2023;82:324–30.
- [102] Ytterberg SR, Bhatt DL, Mikuls TR, Koch GG, Fleischmann R, Rivas JL, Germino R, Menon S, Sun Y, Wang C, Shapiro AB, Kanik KS, Connell CA. Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. *N Engl J Med* 2022;386:316–26.
- [103] Robertson J, Porter D, Sattar N, Packard CJ, Caslake M, McInnes I, McCarey D. Interleukin-6 blockade raises LDL via reduced catabolism rather than via increased synthesis: a cytokine-specific mechanism for cholesterol changes in rheumatoid arthritis. *Ann Rheum Dis* 2017;76:1949–52.
- [104] Maqsood MH, Weber BN, Haberman RH, Lo Sicco KI, Bangalore S, Garshick MS. Cardiovascular and venous thromboembolic risk with janus kinase inhibitors in immune-mediated inflammatory diseases: a systematic review and meta-analysis of randomized trials. *ACR Open Rheumatol* 2022;4:912–22.
- [105] Shah JT, Shah KT, Femia AN, Lo Sicco KI, Merola JF, Weber B, Garshick MS. Cardiovascular risk management in patients treated with janus kinase inhibitors. *J Cardiovasc Pharmacol* 2024;83:392–402.
- [106] Kearney CA, Saha S, Mata Vivas MT, Gelfand JM, Garelik J, Lo Sicco KI, Garshick M. Characterization of cardiometabolic risk awareness among patients with psoriasis: A quality improvement survey study. *JAAD Int* 2024;16:72–4.
- [107] Garshick MS, Berger JS. Psoriasis and Cardiovascular disease—an ounce of prevention is worth a pound of cure. *JAMA Dermatol* 2022;158:239–41.
- [108] Hall KD, Bemis T, Brychta R, Chen KY, Courville A, Crayner EJ, Goodwin S, Guo J, Howard L, Knuth ND, Miller 3rd BV, Prado CM, Siervo M, Skarulis MC, Walter M, Walter PJ, Yannai L. Calorie for calorie, dietary fat restriction results in more body fat loss than carbohydrate restriction in people with obesity. *Cell Metab* 2015;22:427–36.
- [109] Hall KD, Chen KY, Guo J, Lam YY, Leibel RL, Mayer LE, Reitman ML, Rosenbaum M, Smith SR, Walsh BT, Ravussin E. Energy expenditure and body composition changes after an isocaloric ketogenic diet in overweight and obese men. *Am J Clin Nutr* 2016;104:324–33.
- [110] Hall KD, Guo J, Courville AB, Boring J, Brychta R, Chen KY, Darcey V, Forde CG, Gharib AM, Gallagher I, Howard R, Joseph PV, Milley L, Ouwerkerk R, Raisinger K, Rozga I, Schick A, Stagliano M, Torres S, Walter M, Walter P, Yang S, Chung ST. Effect of a plant-based, low-fat diet versus an animal-based, ketogenic diet on ad libitum energy intake. *Nat Med* 2021;27:344–53.
- [111] Hall KD, Ayuketah A, Brychta R, Cai H, Cassimatis T, Chen KY, Chung ST, Costa E, Courville A, Darcey V, Fletcher LA, Forde CG, Gharib AM, Guo J, Howard R, Joseph PV, McGehee S, Ouwerkerk R, Raisinger K, Rozga I, Stagliano M, Walter M, Walter PJ, Yang S, Zhou M. Ultra-Processed diets cause excess calorie intake and weight gain: an inpatient randomized controlled trial of ad libitum food intake. *Cell Metab* 2019;30:67–77. e3.
- [112] Williams A, Nolan TS, Luthy J, Brewer LC, Ortiz R, Venkatesh KK, Sanchez E, Brock GN, Nawaz S, Garner JA, Walker DM, Gray 2nd DM, Joseph JJ. Association of socioeconomic status with life's essential 8 in the national health and nutrition examination survey: effect modification by sex. *J Am Heart Assoc* 2024;13:e030805.
- [113] Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, Emam A, Parker TL, Vidgen E, Trautwein EA, Lapsley KG, Josse RG, Leiter LA, Singer W, Connelly PW. Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. *Am J Clin Nutr* 2005;81:380–7.
- [114] Glenn AJ, Guasch-Ferré M, Malik VS, Kendall CWC, Manson JE, Rimm EB, Willett WC, Sun Q, Jenkins DJA, Hu FB, Sievenpiper JL. Portfolio diet score and risk of cardiovascular diseases: findings from 3 prospective cohort studies. *Circulation* 2023;148:1750–63.
- [115] Steffen LM, Kroenke CH, Yu X, Pereira MA, Slattery ML, Van Horn L, Gross MD, Jacobs Jr DR. Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr* 2005;82:1169–77. quiz 1363-4.
- [116] Neal B, Wu Y, Feng X, Zhang R, Zhang Y, Shi J, Zhang J, Tian M, Huang L, Li Z, Yu Y, Zhao Y, Zhou B, Sun J, Liu Y, Yin X, Hao Z, Yu J, Li KC, Zhang X, Duan P, Wang F, Ma B, Shi W, Di Tanna GL, Stepien S, Shan S, Pearson SA, Li N, Yan LL, Labarthe D, Elliott P. Effect of salt substitution on cardiovascular events and death. *N Engl J Med* 2021;385:1067–77.
- [117] Tonstad S, Butler T, Yan R, Fraser GE. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care* 2009;32:791–6.
- [118] Sullivan VK, Kim H, Caulfield LE, Steffen LM, Selvin E, Rebholz CM. Plant-based dietary patterns and incident diabetes in the atherosclerosis risk in communities (aric) study. *Diabetes Care* 2024;47:803–9.
- [119] Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Böck M, Benetos A, Biffi A, Boavida JM, Capodanno D, Cosyns B, Crawford C, Davos CH, Desormais I, Di Angelantonio E, Franco OH, Halvorsen S, Hobbs FDR, Hollander M, Jankowska EA, Michal M, Sacco S, Sattar N, Tokgozoglu L, Tonstad S, Tsioufis KP, van Dis I, van Gelder IC, Wanner C, Williams B. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2021;42:3227–337.
- [120] Corbin KD, Carnero EA, Dirks B, Igudesman D, Yi F, Marcus A, Davis TL, Pratley RE, Rittmann BE, Krajmalnik-Brown R, Smith SR. Host-diet-gut microbiome interactions influence human energy balance: a randomized clinical trial. *Nat Commun* 2023;14:3161.
- [121] Robinson E, Boyland E, Chisholm A, Harrold J, Maloney NG, Marty L, Mead BR, Noonan R, Hardman CA. Obesity, eating behavior and physical activity during COVID-19 lockdown: a study of UK adults. *Appetite* 2021;156:104853.
- [122] Simpson HC, Simpson RW, Lousley S, Carter RD, Geekie M, Hockaday TD, Mann JI. A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet* 1981;1:1–5.