UC San Diego Health

The Future of Prevention: Middle Life and Beyond

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Disclosures

- Consultant to: Amgen, Arrowhead, Cleerly, Boehringer Ingelheim, HeartFlow, Lilly, Novo Nordisk, Novartis, Medtronic, Roche, and Corcept.

Research Funding/ Grants:

- NIH R01 DK118278 and 2R01DK118278-06A1: (PI: Taub PR) (NCT0405733)
- Hillblom Network Grant (PI: Taub PR) (NCT05365529)
- NIH RECOVER OT2HL156812

Executive Steering Committee Member for Clinical Trials:

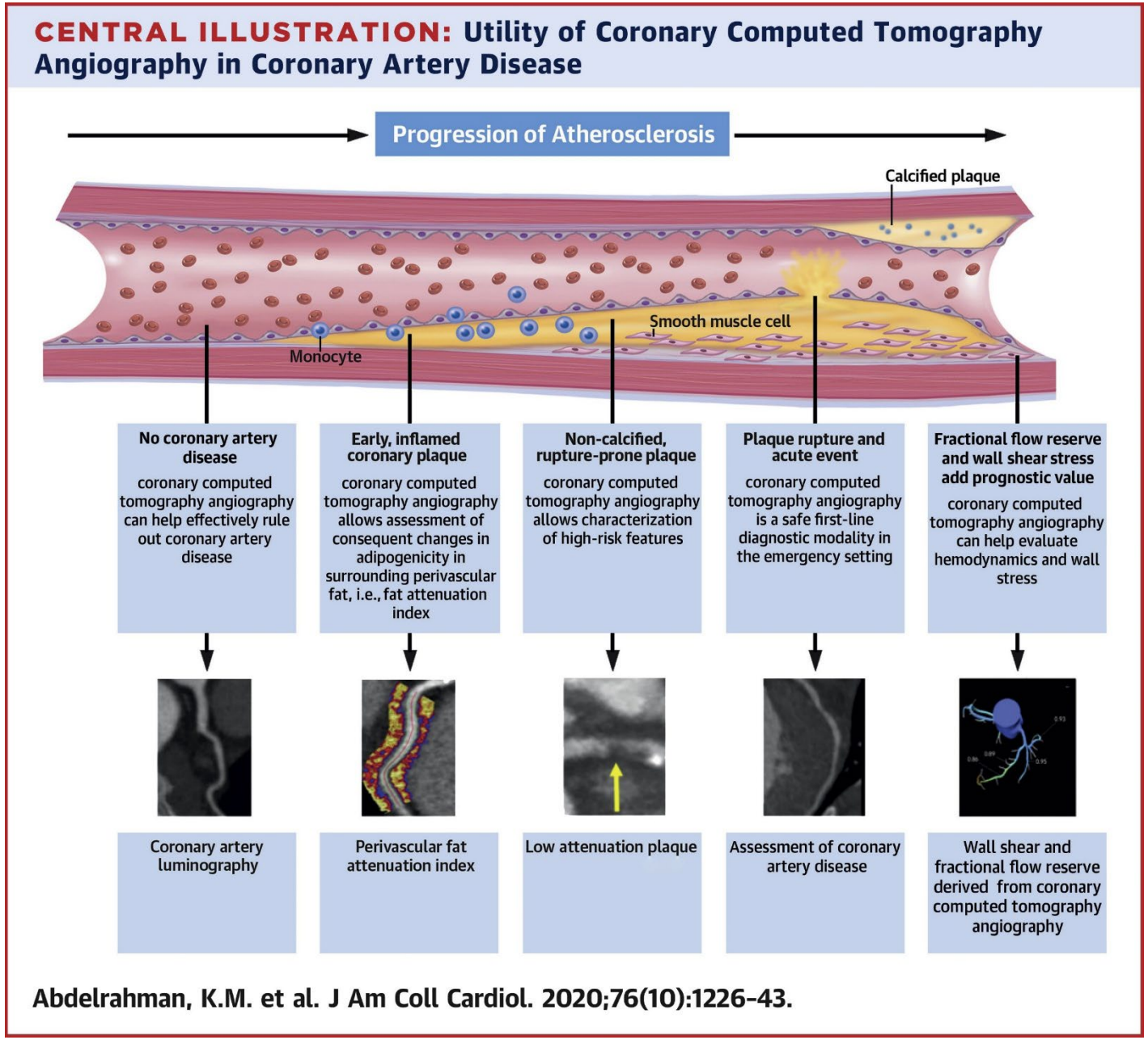
- VICTORIAN-1P, *Sponsor: Novartis; NCT 05739383*
- TRANSFORM Trial, *Sponsor: Cleerly; NCT 06112418*
- SPYRAL GEMINI: Sponsor: *Medtronic; NCT06907147*
- EASi-PROTKT Trial, *Sponsor: Boehringer Ingelheim; NCT07064473*
- AMBIENCE CVOT of Zenagamtide, *Sponsor: Novo Nordisk*
- Global Phase 3 Study of CT-388 (GLP-1/GIP receptor agonist) *Sponsor:Roche*
- *Global Phase 3 CVOT with Resmetirom Sponsor: Madrigal*
- DII235 in Adults With Elevated Lipoprotein(a) *Sponsor: Novartis*

US National Lead/Steering Committee Member:

- VICTORION-2P CVOT, *Sponsor: Novartis; NCT 05030428*
- Ocean(a) Lp(a) lowering CVOT, *Sponsor: Amgen; NCT 05581303*
- Oral PCSK9 Inhibitor CVOT (MK- 0616), *Sponsor: Merck; NCT 06008756*
- ACCLAIM Lp(a) lowering CVOT, *Sponsor: Lilly NCT06292013*

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There is a Continuum in ASCVD



Continuum of ASCVD Risk

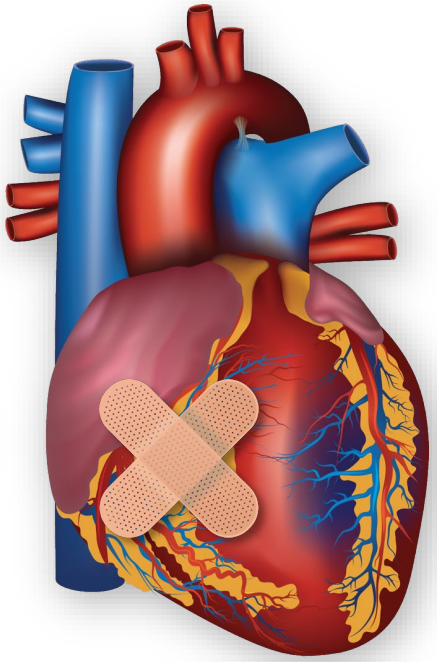


Primary Prevention



High Risk Primary Prevention

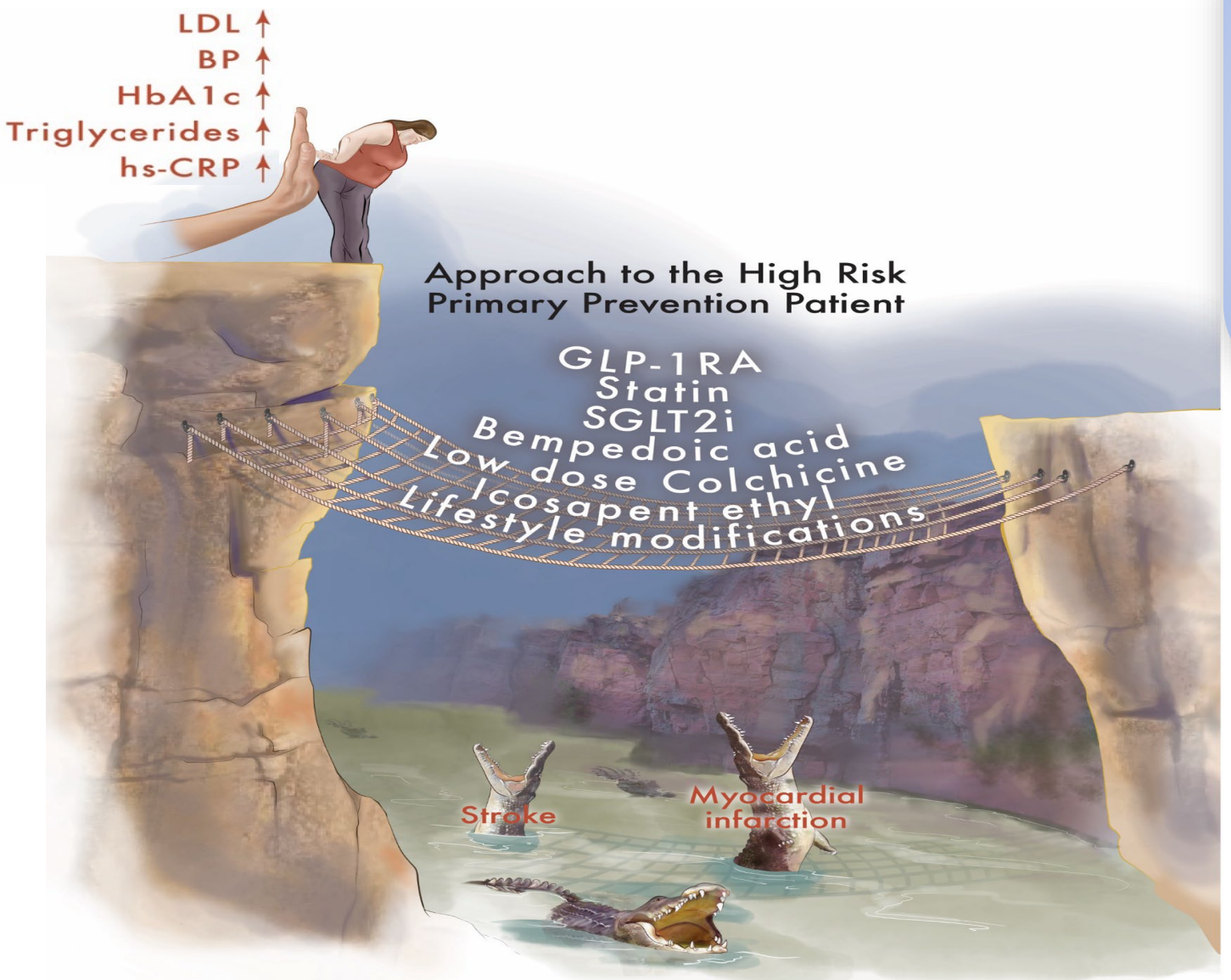
Advanced Subclinical Atherosclerosis?



Secondary Prevention

Blaha MJ, *AJC* 2016

High Risk Primary Prevention (HRPP) Patients: The New Paradigm



What's next for high-risk primary prevention?

- PCSK9i (VESALIUS) & inclisiran (VICTORIAN-1 PREVENT)
- Lp(a) lowering therapies (ACCLAIM, PreEVENT)?
- Triglyceride-lowering therapies?

Ahlers M.…Taub P. Am J Prev Cardiol. 2025 Aug 22;23:101265

Look at How Far we Have Come with Good Mechanistic Understanding

Middle Ages

Leeches used for “bloodletting” to treat many illnesses



From empiric use to evidence-based, targeted therapy

Today

Leeches used in reconstructive surgery to improve wound healing



Then: Empiric and non-specific use

- Believed to “balance humors” or remove “bad blood”
- Used for a wide range of conditions with no mechanistic rationale
- Variable and unpredictable effects

Now: Mechanistically guided, targeted use

- Leech saliva contains bioactive molecules with defined mechanisms
- Hirudin (anticoagulant), vasodilators, anti-inflammatory and antimicrobial peptides
- Improves venous congestion and promotes wound healing in reconstructive surgery (e.g., reattached digits, flaps)

Data can be Used Incorrectly or Precisely



Children of Thalidomide

Thalidomide: Repurposed to Treat Multiple Myeloma

An immunomodulatory drug that targets malignant plasma cells

1 DRUG TARGET

THALIDOMIDE



Binds cereblon (CRBN) in the E3 ubiquitin ligase complex

2 MECHANISM

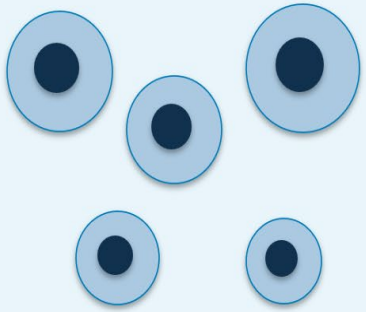
IKZF1 / IKZF3

↓

IRF4 / MYC

Proteasomal degradation and reduced myeloma-cell survival

3 CLINICAL EFFECT



Anti-myeloma activity

Sources: THALOMID prescribing information (DailyMed); PMID: 27492707, 34834536

TOO MUCH DATA: GARBAGE IN and GARBAGE OUT and NOT ACTIONABLE

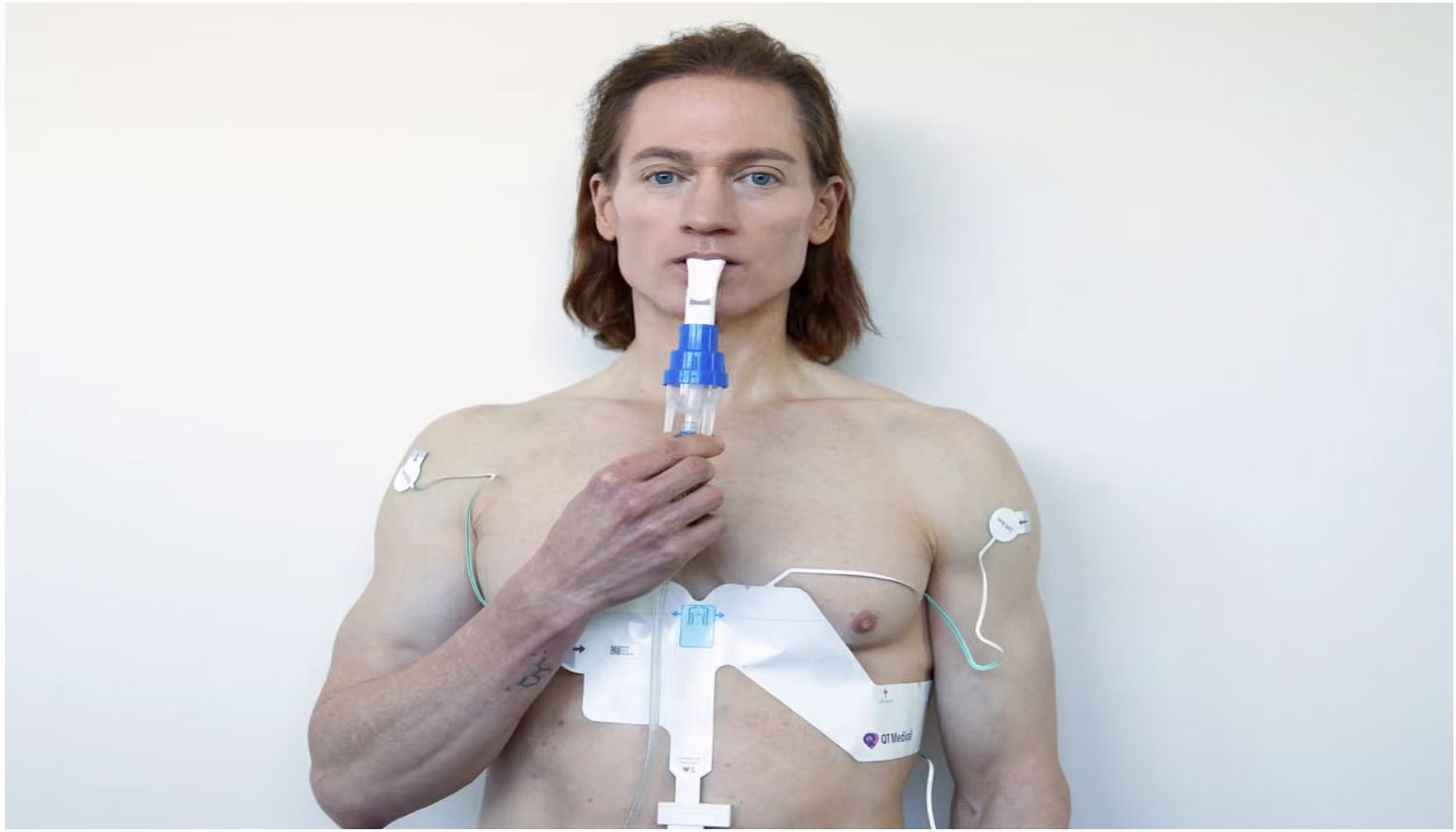
Need to Gather the Right Data and Act on It



‘My ultimate goal? Don’t die’: Bryan Johnson on his controversial plan to live for ever

Joel Snape

The tech entrepreneur is waging a one-man war against ageing. But is taking 100 pills a day, finishing your meals by 11am, giving up both alcohol and a social life, really worth it?



Is This Longevity? Demented and in Diapers?

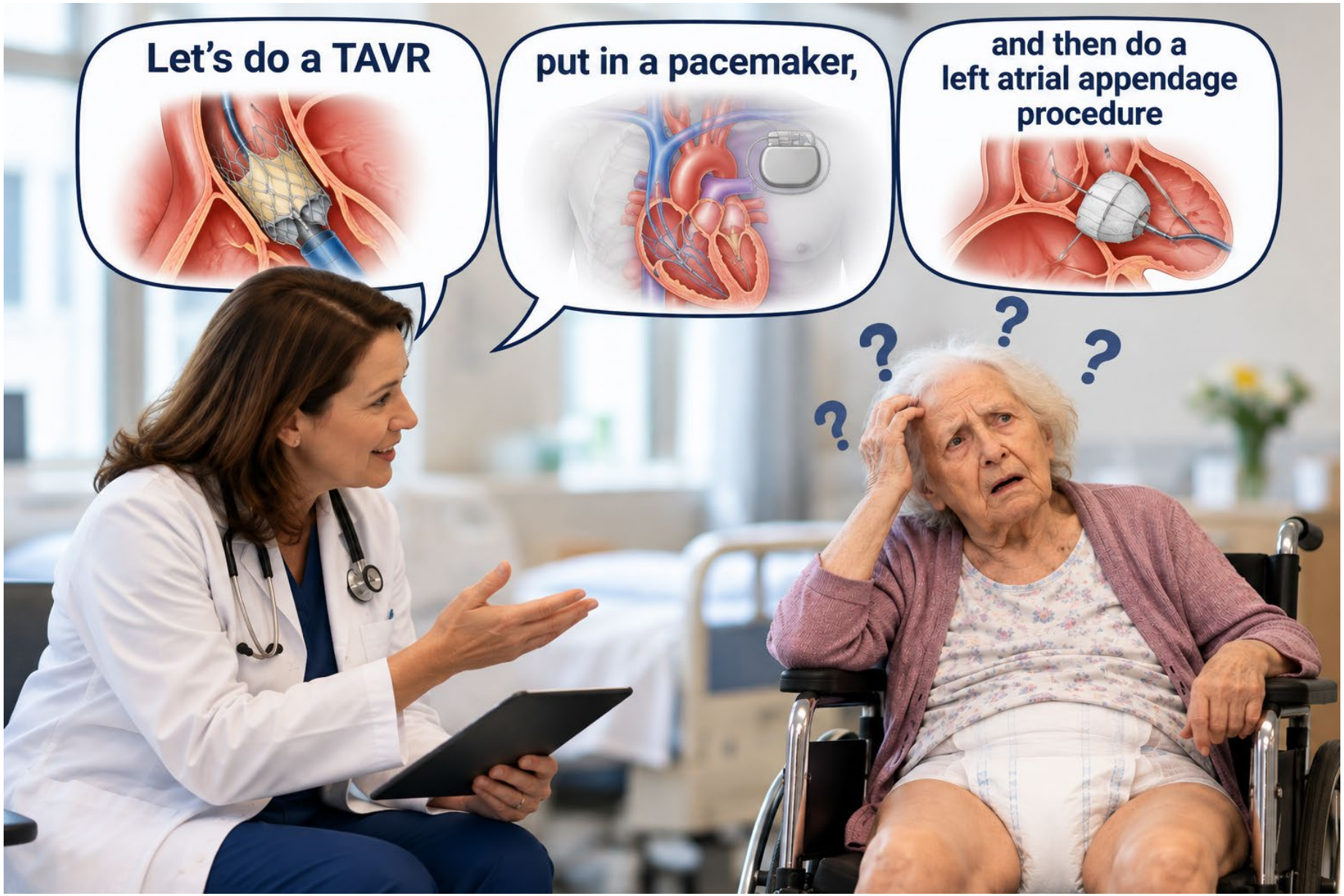
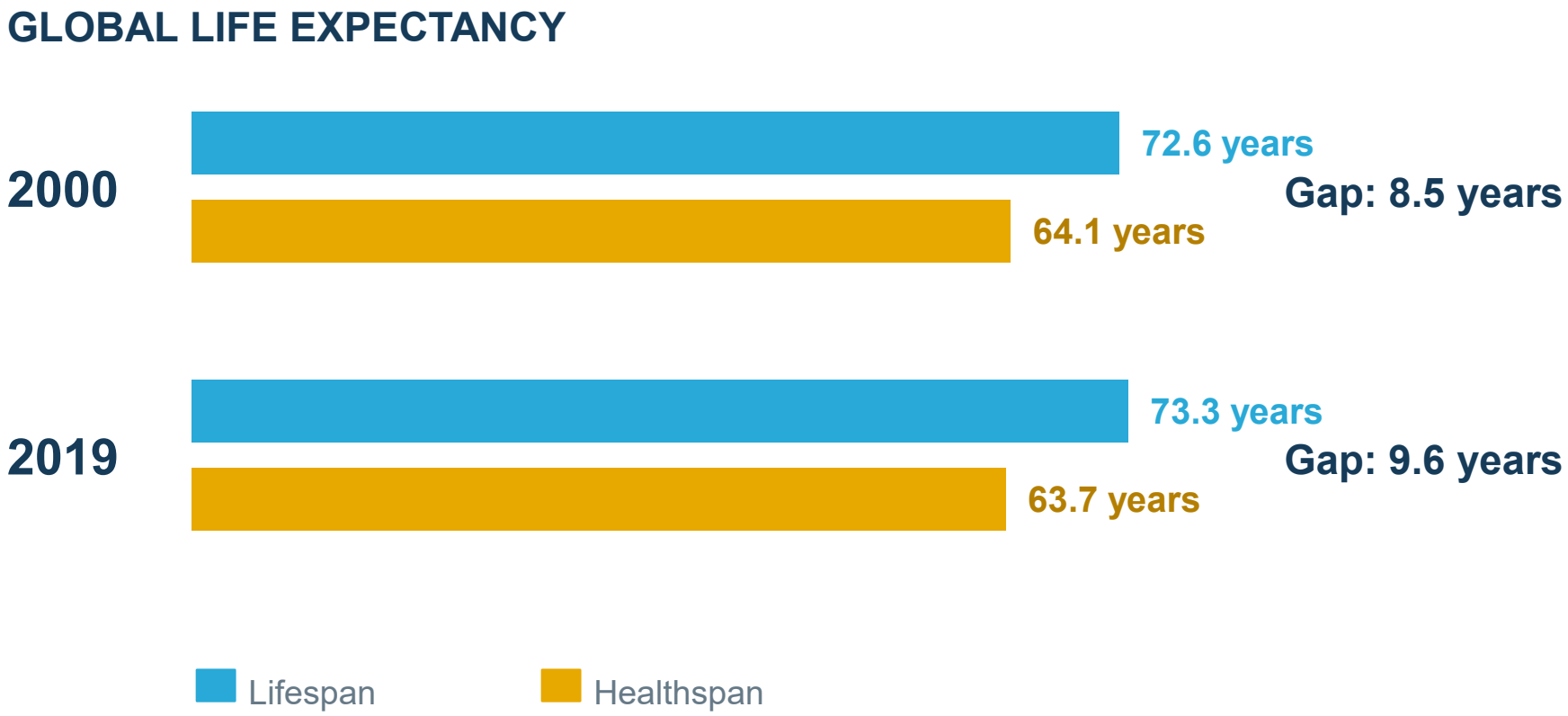


Photo created by AI

Living Longer Does Not Mean Living Healthier

Gains in life expectancy have outpaced gains in healthy life expectancy



The opportunity: prevent disease earlier so added years are healthier years.

Source: Garmany et al. JAMA Network Open. 2024; Global Burden of Disease 2019.

AI Is Shifting Cardiovascular Prevention Earlier

From invisible biology to clinical events, AI can identify risk before traditional recognition.

MOLECULAR CHANGES
Invisible biology

>

SUBCLINICAL DISEASE
Structural and physiologic changes

>

DETECTABLE DISEASE
Imaging, ECG, biomarkers

>

SYMPTOMS
Clinical recognition

>

EVENTS
Myocardial infarction
Stroke • Heart failure
Aortic disease



1 AI-Enabled ECG Biomarkers

Detect signals not seen by the human eye



- Deep learning applied to large ECG datasets
- Predicts future hypertension, heart failure, myocardial infarction and stroke
- Independent of conventional risk factors

2 Cardiovascular Foundation Models

Learn generalizable representations of cardiovascular physiology



- Pretrained on millions of multimodal datasets (ECG, imaging, biomarkers, genetics)
- Support multiple cardiovascular prediction tasks
- Capture shared disease biology across conditions

3 Multimodal Prediction

Integrate ECG, imaging, biomarkers and clinical data



The future of prevention is identifying cardiovascular disease before symptoms or clinical events occur.

UC San Diego Health

Why do most clinicians rely on single blood pressure readings in the office and other episodic measurements to make treatment decisions?



From Episodic Care to Continuous, Intelligent Prevention

Leveraging real-world data and AI to understand where the patient is now and where they are headed.

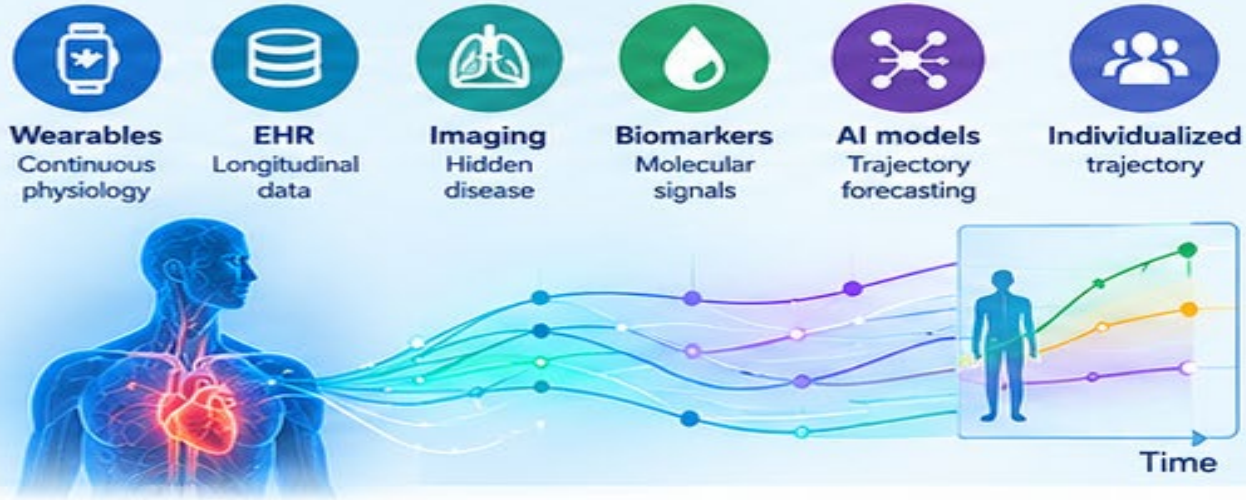
Episodic Medicine

A snapshot in time – we measure, calculate and act, and then often lose sight of the trajectory.



Intelligent Prevention

Continuous data, AI models and multimodal information to understand where the patient is – and where they are headed.



Emerging Opportunity: Digital Twins

Continuously updated computational models that integrate multimodal data to simulate disease trajectories and test the potential impact of interventions.



The goal is not a digital copy of the patient.

It is the ability to ask: which future are we headed toward — and which intervention changes that future?

Blood Finger Sticks Are Outdated! CGM Gives us More Dynamic Insights



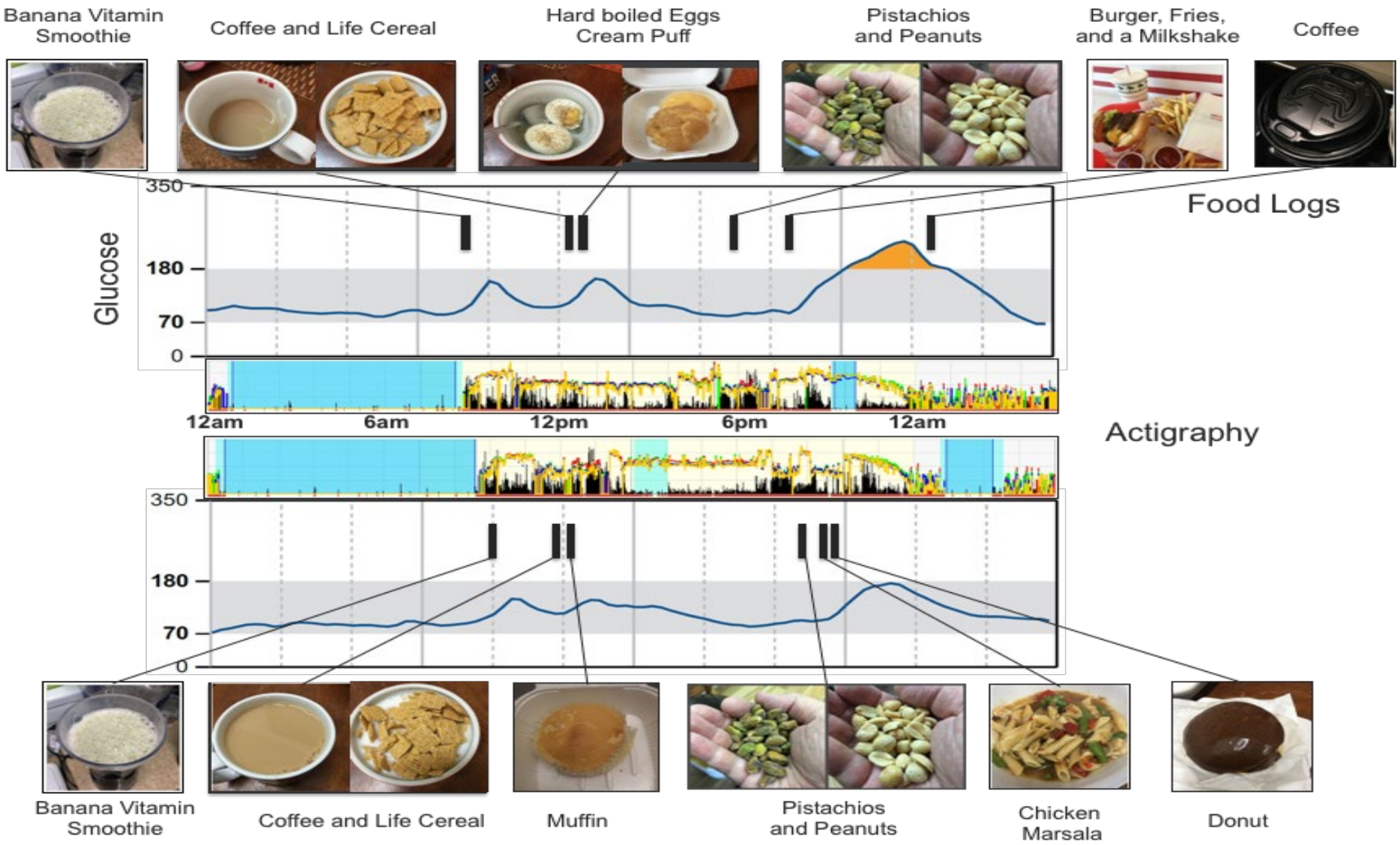






Erbach M, et al. J Diabetes Sci Technol. 2016 Aug 22;10(5):1161-8.

Insights into Metabolism Through Continuous Glucose Monitoring (CGM) Need to Move Beyond HbA1c



Wilkinson MJ,…Taub PR *Cell Metabolism* 2020 Jan 7;31(1):92-104

Wearables and other devices need to generate data showing that using them changes clinical parameters before they are widely recommended for patients.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Continuous Glucose Monitoring in Non–Insulin-Treated Type 2 Diabetes

RESULTS

A total of 145 participants were assigned to the CGM group, and 138 to the routine-care group. Participants ranged in age from 21 to 84 years. The mean (±SD) glycated hemoglobin level decreased from 8.8±1.3% at baseline to 7.2±1.1% at 26 weeks in the CGM group and from 8.7±1.2% to 8.0±1.4% in the routine-care group (adjusted mean difference, −0.9 percentage points; 95% confidence interval [CI], −1.1 to −0.6; P<0.001). The mean percentage of time that the CGM-measured glucose level was in the glucose-level range of 70 to 180 mg per deciliter was 21 percentage points higher (95% CI, 16 to 26) with CGM than with routine care (P<0.001). The between-group difference in the percentage of time that the glucose level was below 54 mg per deciliter was −0.17 percentage points (95% CI, −0.27 to −0.11; P<0.001 for noninferiority); the difference in the percentage of time that the glucose level was below 70 mg per deciliter was −0.20 percentage points (95% CI, −0.43 to −0.09; P<0.001 for noninferiority; P=0.004 for superiority). No severe hypoglycemia events were reported.

CONCLUSIONS

Among adults with type 2 diabetes that was not being treated with insulin and was being managed in a primary care setting, the use of CGM led to a greater reduction in the glycated hemoglobin level and to a lower risk of hyperglycemia than routine care. (Funded by Dexcom; CONNECT ClinicalTrials.gov number, NCT06601166.)

Medicare Annual Wellness Visit (Checkup)

A preventive visit to assess your health, identify risks, and create a personalized prevention plan

Who and When?

65

Age 65

Eligible for Medicare and can have a **Welcome to Medicare** visit (within first 12 months of Part B)

12+ months

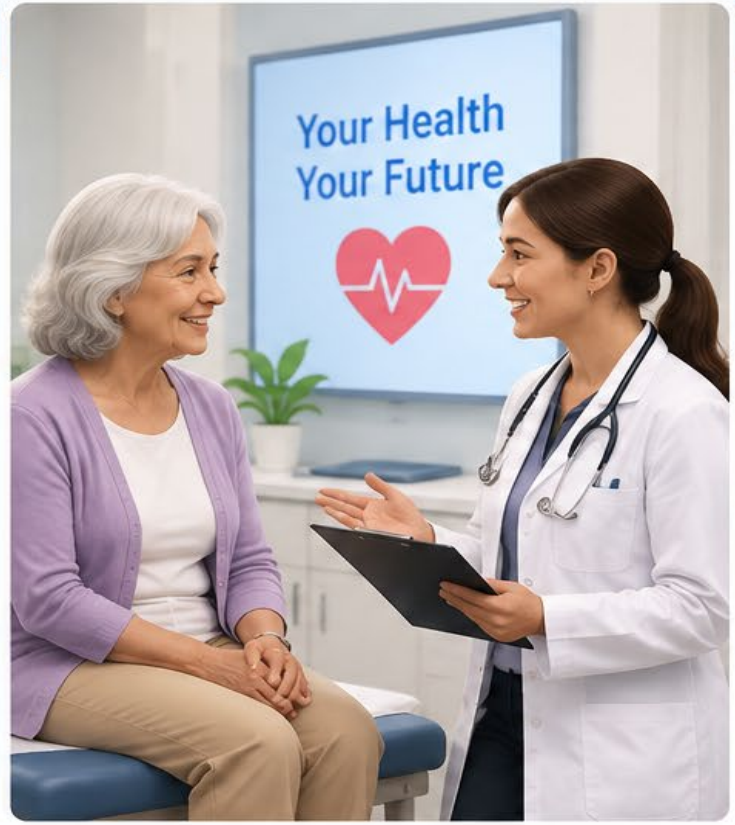
Age 66 and beyond

Annual Wellness Visit once you have had Medicare Part B for at least 12 months

12 months

Every 12 months

Subsequent Annual Wellness Visit



What's Included?

- **Medical history** — Conditions, surgeries, hospitalizations, family history
- **Medication review** — Prescriptions, OTC medications, supplements
- **Vital signs** — Blood pressure, height, weight, BMI
- **Cognitive screening** — Assessment for memory impairment
- **Cardiovascular risk** — Hypertension, diabetes, dyslipidemia, smoking, obesity and other risk factors
- **Depression screening** — Assessment of mood and mental health
- **Fall risk assessment** — Falls, balance, mobility, home safety
- **Functional assessment** — Activities of daily living (e.g., dressing, bathing, managing medications)
- **Lifestyle assessment** — Diet, exercise, tobacco and alcohol use
- **Preventive screening review** — Cancer screening, osteoporosis screening, immunizations, and other age-appropriate services
- **Advance care planning** — Discussion of advance directives and healthcare preferences
- **Personalized prevention plan** — Written recommendations and a schedule of preventive services

What's NOT Routinely Included?

- Comprehensive head-to-toe physical examination
- ECG
- Routine blood tests (e.g., cholesterol, glucose, etc.)
- Evaluation and management of new or worsening medical problems

These services may be performed when clinically indicated, but coverage and cost-sharing depend on the service and diagnosis.

Coverage

Generally covered at no out-of-pocket cost under Medicare Part B when the provider accepts assignment.

Additional diagnostic or problem-oriented services may result in charges.

Instead of a Medicare Wellness Visit...



Traditional Medicare Checkup Focuses On:

- ☐ Medical history
- ☐ Medication review
- ☐ Basic vital signs
- ☐ Cognitive screening
- ☐ Depression screening
- ☐ Fall risk
- ☐ Review of preventive screenings and vaccines

Let's Envision a Middle Age Prevention Visit.

Age 40 – 45

Proactive, personalized, evidence-based care to help you stay healthy, active and independent for decades to come.



Check Evidence-Based Biomarkers



- Lp(a) – lifetime risk for ASCVD and aortic stenosis
- Lipid panel (ApoB, LDL-C, non-HDL-C)
- hs-CRP (inflammation)
- A1c (glycemia)
- Other markers as indicated (e.g., lipoprotein(a), NT-proBNP)

Consider CGM and other wearable data inputs to provide Real-time insights



- Continuous glucose monitoring (CGM)
- Other wearable data inputs (e.g., ring that tracks sleep, activity, heart rate, HRV)
- Understand real-time data patterns (glucose, sleep, activity, stress, recovery)
- Personalized dietary and lifestyle insights

Check Body Composition



Body Fat	28%
Lean Mass	68%
Visceral Fat	Low
Bone Density	Normal

- Body composition analysis (e.g., DEXA or BIA)
- Assess body fat, lean mass and visceral fat
- Evaluate bone health (especially in women)
- Guide personalized exercise and nutrition plans

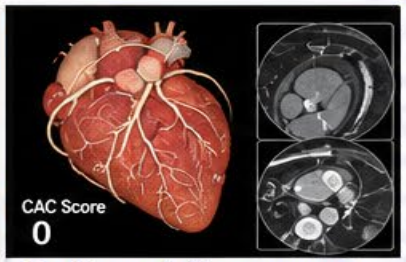
Check Strength, Fitness and VO_2 Max



- Cardiorespiratory fitness (VO_2 max)
- Muscle strength (e.g., grip strength, functional testing)
- Balance and mobility assessment
- Identify areas to improve fitness, strength and longevity

Advanced Risk Assessment

(e.g., CAC score or CTA coronary when appropriate)



- Advanced risk assessment (e.g., CAC score or CTA coronary when appropriate)
- Blood pressure (including home or ambulatory BP)
- Heart rhythm screening (e.g., ECG)
- Personalized risk reduction plan (lipids, blood pressure, diabetes, lifestyle and other therapies)

Assess Brain, Mental and Overall Health



- Cognitive health screening
- Mental health and stress assessment
- Sleep evaluation
- Menopause and hormonal health (when relevant)
- Vaccinations and age-appropriate cancer screening
- Develop a personalized prevention plan

GOAL
Prevent disease.
Optimize healthspan.
Stay active and independent.

PERSONALIZED PLAN
Evidence-based recommendations for nutrition, exercise, risk factor control, and appropriate screening.

A HEALTHIER FUTURE
More years of things you love.


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Jacobs Medical Center