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Dietary rhythms and biological aging risk across multiple organs

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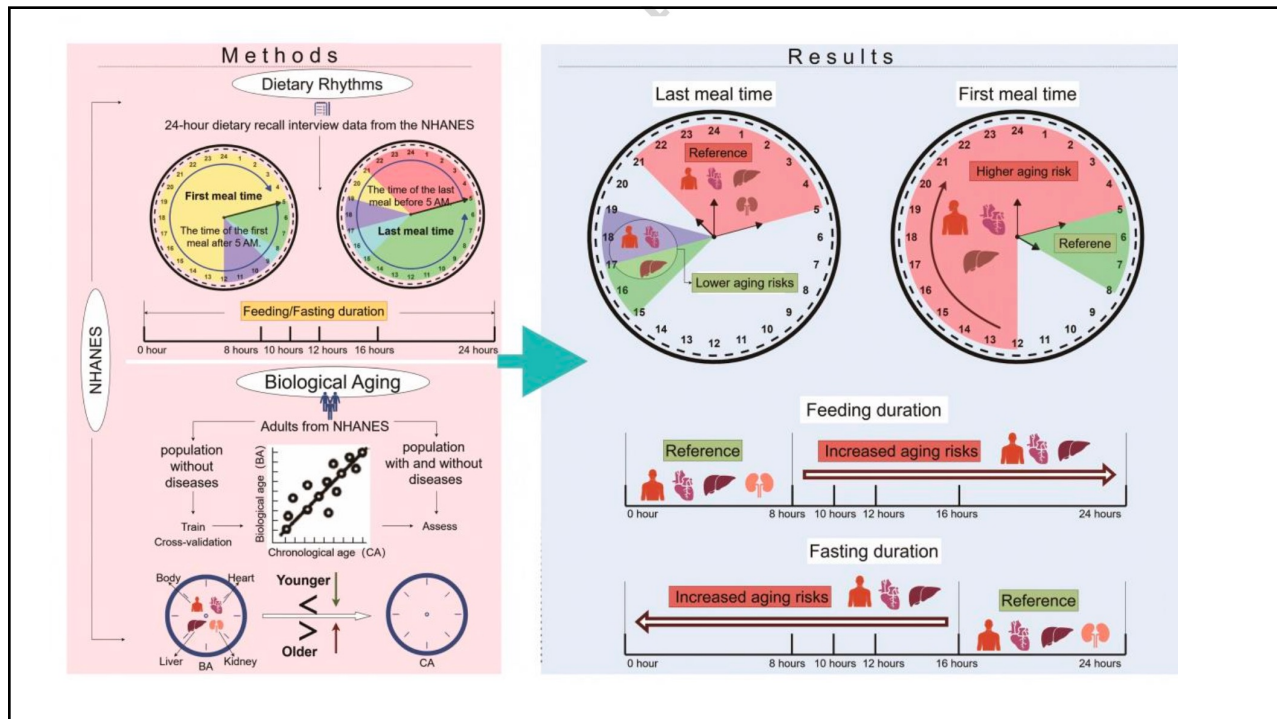
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We are providing an unedited version of this manuscript to give early access to its findings. Before final publication, the manuscript will undergo further editing. Please note there may be errors present which affect the content, and all legal disclaimers apply.

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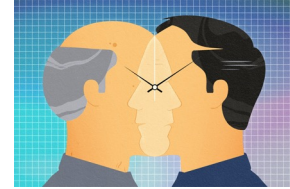
Biologic Clock Measures



- Epigenetic Clocks (3 generations)
- Functional Biologic Aging Clocks
 1. *The Klemmer-Doubal Method (KDM)*
 2. *PhenoAge*

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The Klemera-Doubal method (KDM)



- Biologic age measure is generally considered more accurate than first-generation epigenetic clocks (e.g., Horvath, Hannum) at predicting health outcomes, mortality, and physiological decline, while being roughly comparable to or slightly better than some second-generation epigenetic clocks.
- While epigenetic clocks excel at predicting *chronological* age with high precision, KDM is superior at capturing functional, organ-level aging by utilizing clinical blood biomarkers.
- KDM Biological Age (Physiological Approach)
- Methodology: Combines multiple clinical blood markers (e.g., blood pressure, blood glucose, kidney function) using the Klemera and Doubal (2006) algorithm.
- Strengths: Better at predicting healthspan-related characteristics, such as mortality, functional difficulties, and cognitive decline.

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Key Components of Phenotypic Age (PhenoAge)



- Developed by experts including Morgan Levine and Steve Horvath, the formula relies on nine biomarkers to calculate biological age
- Albumin: A protein indicating liver/kidney health and nutrition.
- Creatinine: A measure of kidney function.
- Glucose: A measure of metabolic health.
- C-Reactive Protein (CRP): A marker of inflammation.
- Lymphocyte Percent: A measure of immune system health.
- Mean Cell Volume (MCV): A measure of red blood cell size.
- Red Cell Distribution Width (RDW): A measure of variability in red blood cell size.
- Alkaline Phosphatase: A liver/bone health enzyme.
- White Blood Cell Count: A measure of total immune cells.
- Chronological Age: The actual age of the person.

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Testing for Biologic Aging Clocks



- Epigenetic Biological Age (DNAm Clocks)
- Methodology: Measures DNA methylation (DNAm) levels at specific CpG sites on the genome.
- Strengths: Highly reliable and consistent in predicting *chronological* age across different populations and tissues.
- Weakness: First-generation clocks have a moderate ability to predict disease.
- Comparison of Accuracy and Performance
- Mortality Prediction: Studies show *KDM* often outperforms early epigenetic clocks in predicting mortality, whereas epigenetic clocks are superior at assessing how closely a person's biological age aligns with their birthdate.
- Sensitivity to Health Changes: *KDM* tends to show stronger associations with health span-related markers than early epigenetic clocks.
- 3rd Generation (DunedinPACE): Newer third-generation epigenetic clocks, such as DunedinPoAm and DunedinPACE, are highly effective, but *KDM* still offers a robust, low-cost, and clinically relevant alternative by reflecting physiological, rather than just cellular, changes.

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For measuring functional/physiological decline and mortality risk, KDM and PhenoAge are often more accurate, while for cellular aging and chronological age estimation, epigenetic clocks are generally more accurate.

- KDM and PhenoAge Predict Mortality: It is a strong predictor of all-cause mortality, as well as deaths from cancer, cardiovascular disease, and respiratory diseases.
- Reflects Lifestyle: Poor health habits can lead to accelerated aging, while maintaining a healthy lifestyle, such as following "Life's Essential 8" (blood pressure, nicotine, diet, activity), can reduce it by roughly 6 years.
- Accessible Measure: Unlike other, more complex tests, PhenoAge can be calculated using standard blood tests (like CMP and CBC) from annual check-ups.

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Review

Timing of Breakfast, Lunch, and Dinner. Effects on Obesity and Metabolic Risk

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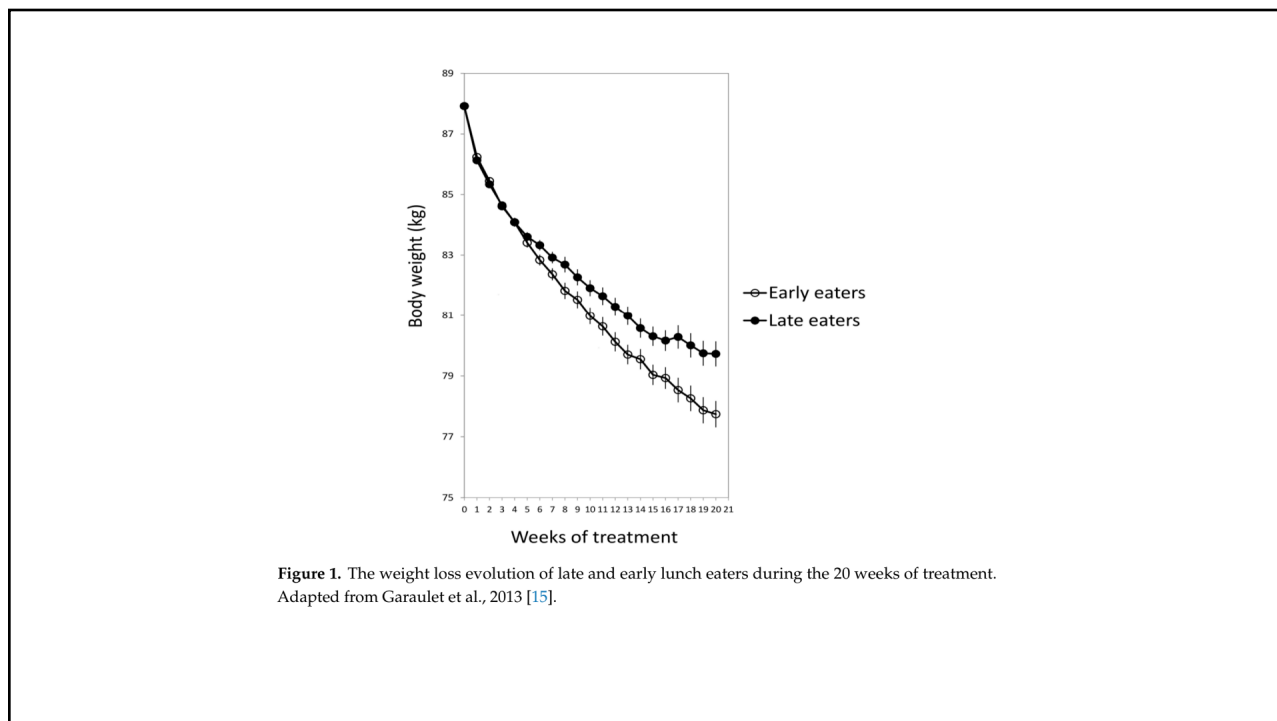
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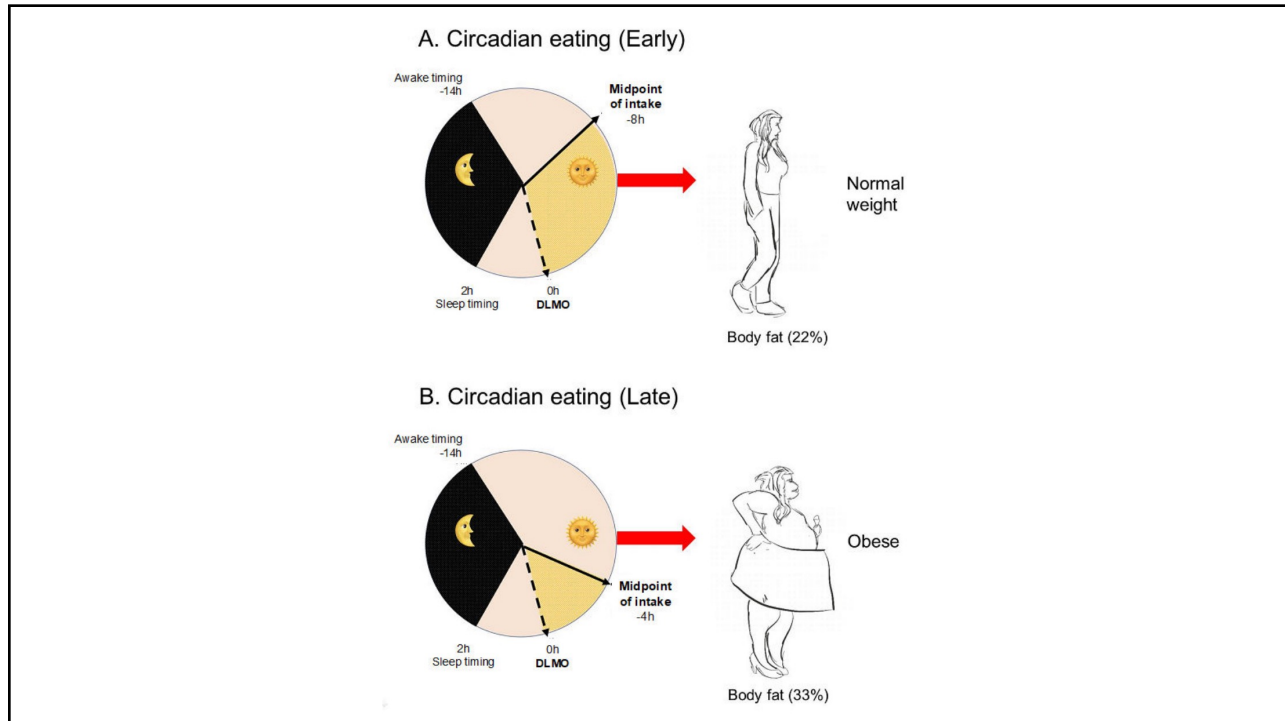
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Abstract: (1) Background: Eating is fundamental to survival. Animals choose when to eat depending on food availability. The timing of eating can synchronize different organs and tissues that are related to food digestion, absorption, or metabolism, such as the stomach, gut, liver, pancreas, or adipose tissue. Studies performed in experimental animal models suggest that food intake is a major external synchronizer of peripheral clocks. Therefore, the timing of eating may be decisive in fat accumulation and mobilization and affect the effectiveness of weight loss treatments. (2) Results: We will review multiple studies about the timing of the three main meals of the day, breakfast, lunch and dinner, and its potential impact on metabolism, glucose tolerance, and obesity-related factors. We will also delve into several mechanisms that may be implicated in the obesogenic effect of eating late. Conclusion: Unusual eating time can produce a disruption in the circadian system that might lead to unhealthy consequences.

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Summary of Research Findings



- Eating breakfast (emphasis on protein/healthy fats) earlier in am after awakening associated with metabolic health benefits. Optimize MPS, insulin-glucose homeostasis, satiety and thermogenesis.
- Eating dinner/supper earlier in day e.g. between 4-7p allowing a fasting period before bedtime for at least 2-3 hours with greatest benefits
- Limiting eating window to < 10-12 hrs/day
- Skipping breakfast and eating a late dinner/snacks close to bedtime is most disruptive to weight, metabolic health, and health span.

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