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Targeting Aging with Metformin (TAME):
A Concrete Plan to Pave the Way for Targeting Aging

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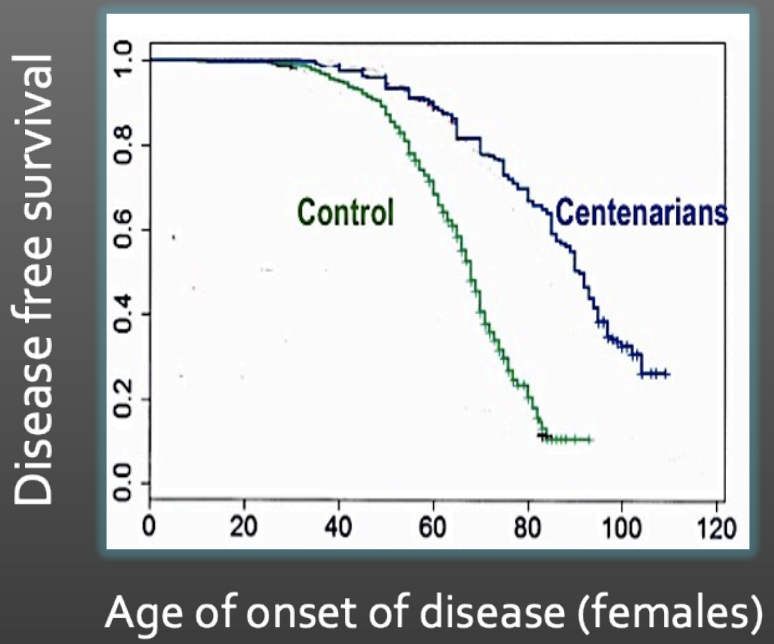
Is it possible to extend healthspan and not only lifespan?

Those living longer also maintain health longer, **even as they grow old**

Centenarians also exhibit compressed morbidity, meaning **fewer years living with disease**, and **economic benefit for society**

Longevity genes have been identified **and have been translated into drugs**



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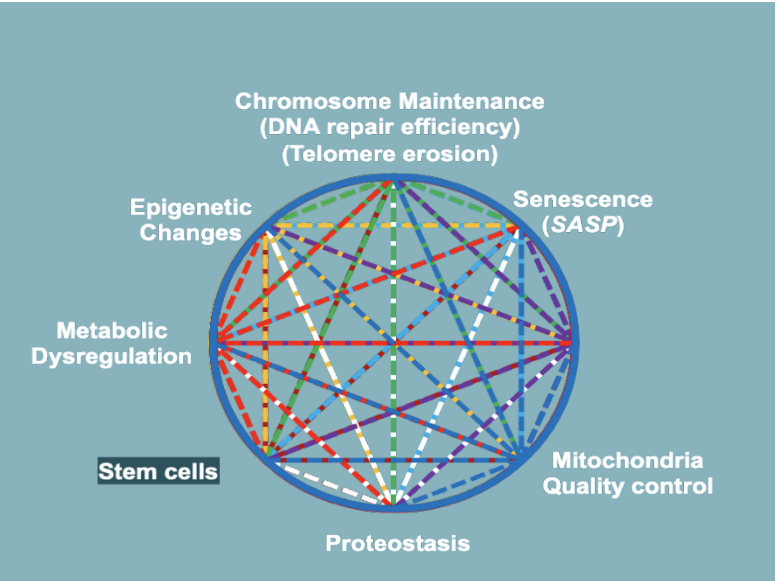
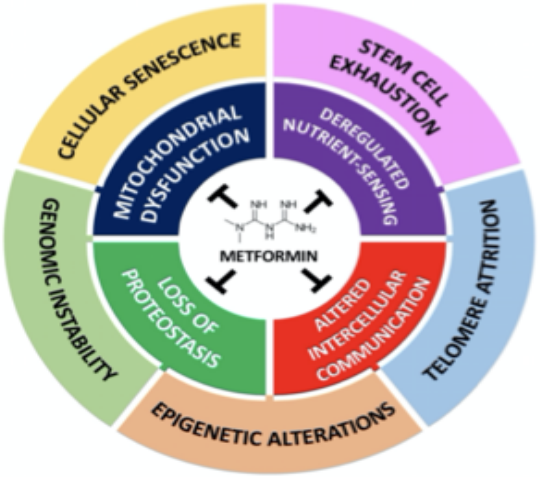
Why do we think we can increase healthspan and lifespan for everyone?

1) Hallmarks of aging provide a theory of promising targets



2) TAME provides the road map necessary for success.



Metformin targets ALL the hallmarks of aging

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What is required for gerotherapeutics in humans:

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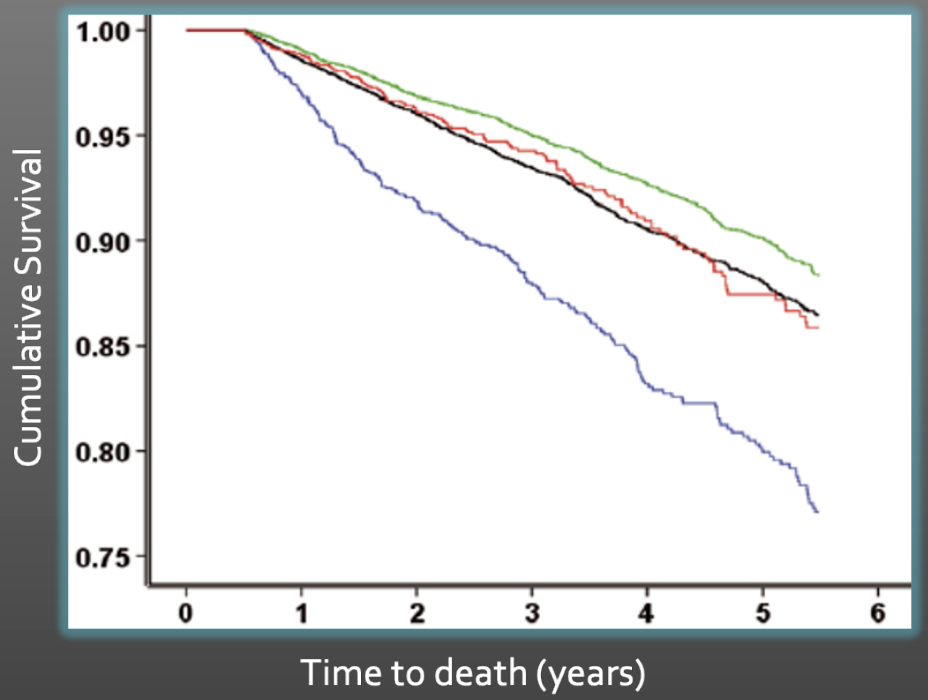
Metformin may be a gerotherapy

There is evidence that drugs like Metformin may decrease mortality, **even in non-diabetics**

If we can demonstrate that **even one drug** can be repurposed as a general-purpose mortality mitigator, **the path for other gerotherpeutics will be cleared**



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Metformin may also have substantial effects on healthspan in humans

Metformin:

- Prevents diabetes (T2DM) (DPP)
- Prevents cardiovascular diseases (UKPDS)
- Is associated with less cancer
- Slow cognitive decline and AD

Thus, metformin is the perfect **tool** for repurposing a gerotherapeutics

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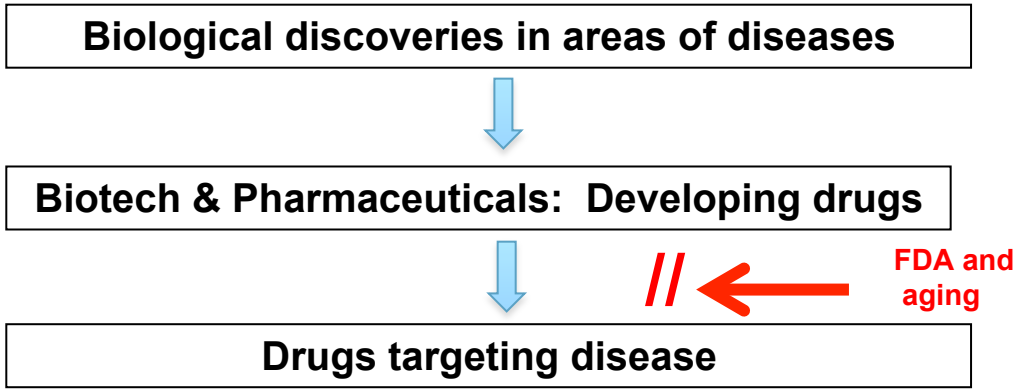
Can we repurpose Metformin to target aging?

If diseases of aging are not **recognized as preventable conditions**:

1) Healthcare provider would not pay for their clients.
2) Pharmaceuticals will not develop other, better and combination of drugs.



TAME Study Design

(In consultation with the FDA)

Inclusion Criteria: Age 65-80

N = 3,000

Double blind placebo-controlled trial

(Clinical) Time to incidence of any major age-related disease:

MI, stroke, cancer*, CHF, MCI/ dementia, or death. FDA

((Biological) Change in metformin levels and biomarkers of aging and age-related diseases NIA.

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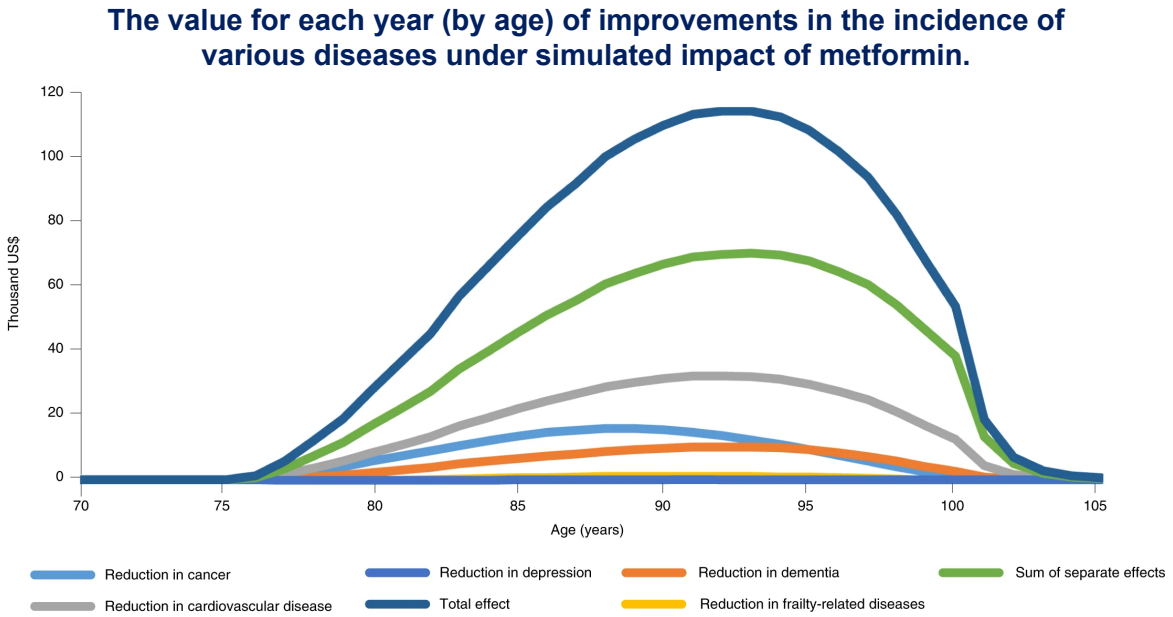
TAME will cost ~$50M, but the economic benefits may mean it pays for itself (~$100M)



AJ Scott et al., The economic value of targeting aging *Nature Aging* (2021)

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FDA Response to TAME

The TAME Study:

- Provide proof of concept that aging **can** be targeted and healthspan **can** be extended
- Inspire the **FDA to make aging an indication**
- **Provide a template** for biotech and pharma of how to move forward with their clinical studies and new biotech opportunities

The TAME Trial infrastructure is ready **today**

01:37:27:08

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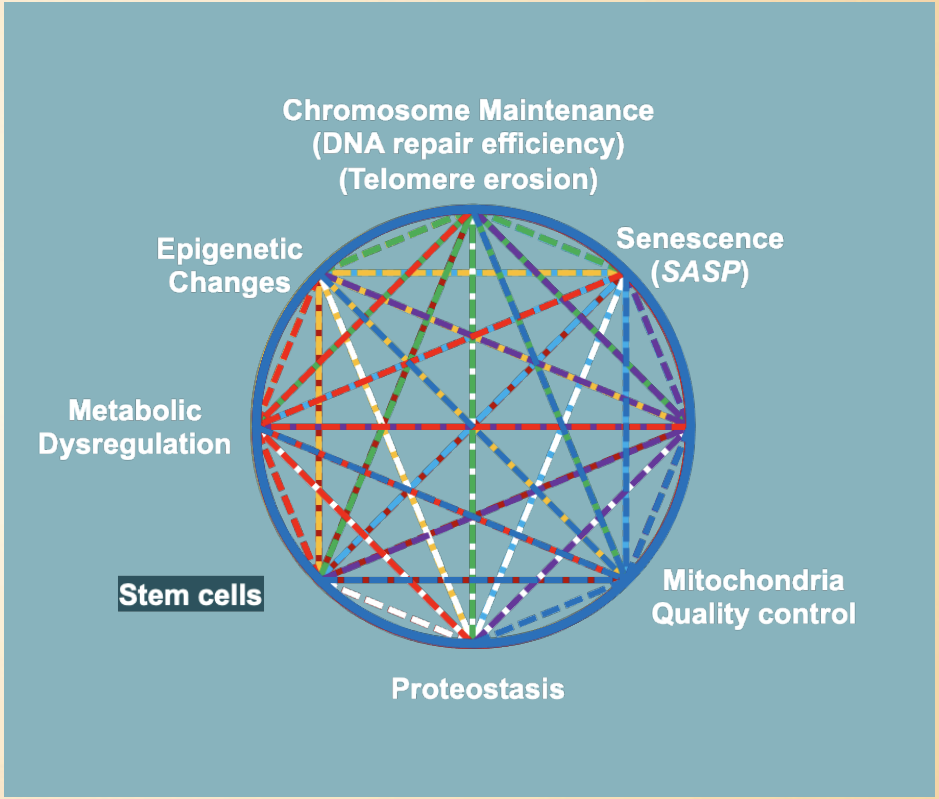
Learn more at www.afar.org/tame-trial

Thank you

The drivers of aging are diverse and **systemic** within the body, defying quantification by a **single measure**

Without a way of **quantifying the progress of aging**, drugs cannot be approved as effective, insurers will never pay for treatments, and drugs targeting aging cannot be developed



By understanding the mechanisms by which a single drug, like Metformin, slows down aging, we will **better understand aging itself**

The performance of other drugs can then be measured against their **influence on these pathways**

TAME is designed to be a pathbreaker for aging therapies

Inclusion Criteria: Ages 65-80, slow gait or incidence of age-related disease

Primary Outcome: Time to incidence of major age-related health outcome

The Goal:

- **Demonstrate broad age-related effects**
- **Capture data on biomarkers of aging**

Thank You

Why should you commit to increased health span and longevity?

Possible definitions:

- Compressed Morbidity
- Aging Reversal
- Total Absence of Evidence of Aging

Life expectancy today is unprecedented relative to the past, and healthspan has **generally increase with it**