Patient Centered Precision (P4) Medicine Is the Future of Geriatric Medicine
Geriatric Workforce

Geriatricians/10,000 population 65 years and over

Decline in Geriatricians in United States

<table>
<thead>
<tr>
<th></th>
<th>1988</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geriatricians</td>
<td>7,128</td>
<td>7,750</td>
</tr>
<tr>
<td>Geriatricians per older adult</td>
<td>1 for every 2,546</td>
<td>1 for every 4,254</td>
</tr>
<tr>
<td>Geropsychiatrists</td>
<td>1,596</td>
<td>1,659</td>
</tr>
<tr>
<td>Geriatric psychiatrists per older adult</td>
<td>1 for every 11,372</td>
<td>1 for every 20,195</td>
</tr>
</tbody>
</table>
George Edward Day  
(1815-1872)

GERIATRICS

“I offer no apology for the publication of this volume. The subject is one of the highest importance, and yet it has been strangely overlooked during the last half-century by the physicians of all countries.”
Effectiveness of a geriatric evaluation unit. A randomized clinical trial. 
Rubenstein LZ, Josephson KR, Wieland GD, English PA, Sayre JA, Kane RL.

At one year, patients who had been assigned to the geriatric unit had much lower mortality than controls (23.8 vs. 48.3 per cent, P less than 0.005) and were less likely to have initially been discharged to a nursing home (12.7 vs. 30.0 per cent, P less than 0.05) or to have spent any time in nursing home (26.9 vs. 46.7 per cent, P less than 0.05).
“The Geriatric Giants”
Professor Bernard Isaacs (1924-1995)

- Instability (Falls)
- Incontinence
- Immobility
- Intellectual impairment

“Geriatricians are certain they are specialists, but uncertain of what they are specialists in” (1981)
Modern Giants of Geriatrics

Frailty

Sarcopenia

Anorexia of Aging

Cognitive Impairment
“I am launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes - and to give us all access to personalized information we need to keep ourselves and our families healthier”

President Obama

State of the Union
January 20, 2015

“An emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment and lifestyle for individuals”

National Institutes of Health
Patient Centered Medicine
Precision Medicine recognizes that different patients need different treatment approaches.

**Standard (Imprecise) Medicine**
- Same approach to heterogeneous clinical presentation and variable clinical outcomes
- One-fits-it-all treatment
- Morbidity and mortality remain high

**Precision Medicine**
- Greater understanding of individual variations in disease pathology
- More precise disease and patient classification
- Targeted and tailored therapeutics

**Patient population**
- Tailored approach
  - Treatment A
  - Treatment B
  - Treatment C
  - Treatment D

**Treatment**
- Standard approach
  - Treatment A (effective in 20% of target population; 80% is waste)
P4 MEDICINE

- Predictive
- Preventive
- Personalized
- Participatory
- Proactive, not reactive
- Focuses on individuals not populations

If you just focus on the smallest details, you will never get the big picture right.

— Larry Hood —
Components of successful ageing

RESILIENCE
the capacity to recover quickly from difficulties; toughness

FRAILTY

Lopez-Otin et al., Cell, 2016
An International Consensus and Assessment for Frailty
Age at which footballers peak

The analysis in this paper employs data from the four major European top flight leagues – the Bundesliga (Germany), Premier League (England), Serie A (Italy) and La Liga (Spain). We use data from the last five seasons, 2010/11 through 2014/15.
FRAILTY DEFINITIONS

“Occurs when under stressful conditions the person has diminished ability to carry out important practiced social activities of daily living. It needs to be distinguished from disability”

Renoir, 1915
Blonde a la rosa
FRAILTY DEFINITION

OBJECTIVE

Fried et al J Gerontol 56A M146,2001

- Weight Loss (10 lbs in 1 year)
- Exhaustion (self-report)
- Weakness (grip strength; lowest 20%)
- Walking speed (15 feet; slowest 20%)
- Low Physical Activity (Kcals/week; lowest 20%)

Female >
Male
6.9%
Biochemistry of Frailty

- Genetic instability
- Telomere attrition
- Epigenetic alterations
- Loss of proteostasis
- Deregulated nutrient sensing
- Mitochondrial dysfunction
- Cellular senescence
- Stem cell exhaustion
- Altered intercellular communication

ERCC1 gene and the proliferating cell nuclear antigen (PCNA) gene are linked to DNA repair as well as increased cancer resistance.
Parabiosis Rejuvenates Old Mice

Muscle
FRAIL
(IANA)

Fatigue
Resistance (Climb 1 flight stairs)
Aerobic (Walk one block)
Illnesses (more than 5 illnesses)
Loss of weight (>5% in 6 months)

1 or 2 PreFRAIL
3 or more FRAIL

>25 VALIDATIONS
Australia (6)
Hong Kong (2)
St Louis (2)
Chicago
China
Chicago
Louisville
Baltimore
Europe (2)
Turkey
Korea
Taiwan
Mexico (2)
Singapore
Brazil
Thailand
9-year OR of ADL deficit or Mortality in persons not lacking ADLs

<table>
<thead>
<tr>
<th>ADLs</th>
<th>PreFrail</th>
<th>Frail</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRAIL</td>
<td>2.74</td>
<td>20.76</td>
<td>.001</td>
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<tr>
<td>SOF</td>
<td>3.09</td>
<td>3.48</td>
<td>.001</td>
</tr>
<tr>
<td>CHS</td>
<td>2.40</td>
<td>6.47</td>
<td>.001</td>
</tr>
<tr>
<td>Rockwood</td>
<td>2.36</td>
<td>5.65</td>
<td>.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MORTALITY</th>
<th>PreFrail</th>
<th>Frail</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.58</td>
<td>3.99</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>1.47</td>
<td>1.40</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>1.35</td>
<td>2.42</td>
<td>.01</td>
<td></td>
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<tr>
<td>2.50</td>
<td>2.66</td>
<td>.001</td>
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</table>
Specificity of Scales in Hong Kong Study

<table>
<thead>
<tr>
<th></th>
<th>MALE</th>
<th>MALE</th>
<th>FEMALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MORTALITY</strong></td>
<td></td>
<td>Physical Limit</td>
<td></td>
<td>Physical Limit</td>
</tr>
<tr>
<td>Rockwood</td>
<td>96.4%</td>
<td>98.4%</td>
<td>93.8%</td>
<td>98%</td>
</tr>
<tr>
<td>CHS</td>
<td>99.2%</td>
<td>100%</td>
<td>99.4%</td>
<td>99.9%</td>
</tr>
<tr>
<td>FRAIL</td>
<td>99.1%</td>
<td>99.4%</td>
<td>99.9%</td>
<td>100%</td>
</tr>
<tr>
<td>Hubbard</td>
<td>98%</td>
<td>99.6%</td>
<td>96.1%</td>
<td>95.1%</td>
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</table>

All had poor Sensitivity
FRAIL Results
7/1/2015 - 6/30/2017

<table>
<thead>
<tr>
<th></th>
<th>Not Frail</th>
<th>Pre-Frail</th>
<th>Frail</th>
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</thead>
<tbody>
<tr>
<td>Physician/Case</td>
<td>33.1%</td>
<td>41.6%</td>
<td>25.3%</td>
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<tr>
<td>Finding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening/Non-</td>
<td>33.8%</td>
<td>44.0%</td>
<td>22.2%</td>
</tr>
<tr>
<td>Physician</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nursing Home</td>
<td>6.0%</td>
<td>22.3%</td>
<td>71.7%</td>
</tr>
<tr>
<td>PACE</td>
<td>11.6%</td>
<td>41.9%</td>
<td>46.5%</td>
</tr>
</tbody>
</table>
Algorithm for Management of Frailty

**Fatigue**
- SLU “AM SAD” for depression
- Do you stop breathing while asleep? Sleep apnea
- TSH for hypothyroid
- Vitamin B12
- Hemoglobin for anemia
- Blood pressure for hypotension/orthostasis

**Resistance Aerobic**
- SARCOPENIA
  - Resistance exercise
  - Aerobic exercise
  - Protein supplement daily
  - 1000 IU vitamin D daily
  - 3 to 5 x week

**Illnesses**
- Review medication list for unnecessary side effects and drugs whose side effects may be contributing to frailty, e.g., anticholinergic drugs

**Loss of Weight**
- Medications producing anorexia
- Emotional – depression
- Abuse, elderly, alcoholism
- Late life paranoia
- Swallowing problems
- Oral problems
- Nosocomial infections, eg, H Pylori
- Wandering and other dementia-related problems
- Hyperthyroidism, hypercalcemia, hyperglycemia, hypoadrenalism
- Enteral problems, eg, celiac disease
- Eating problems
- Low salt, sugar and cholesterol diets
- Stones - cholecystitis

**Caloric Supplementation**
The Polypharmacy Conundrum

Effect of Medication Reduction
Meds reduced from 13.1 to 8.2

Hospitalizations
p<0.0002

Deaths
N.S.
Nutritional, Physical, Cognitive, and Combination Interventions and Frailty Reversal Among Older Adults: A Randomized Controlled Trial

The American Journal of Medicine, Volume 128, Issue 11, 2015, 1225–1236.e1
A multicomponent exercise intervention that reverses frailty
Tarazona-Santabalina et al, JAMDA

**WARM-UP**

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20R each arm</td>
</tr>
<tr>
<td>2</td>
<td>20R each arm</td>
</tr>
<tr>
<td>3</td>
<td>20R each leg</td>
</tr>
<tr>
<td>4</td>
<td>20R each leg</td>
</tr>
<tr>
<td>5</td>
<td>20R each leg</td>
</tr>
<tr>
<td>6</td>
<td>20R each leg</td>
</tr>
</tbody>
</table>

**PROPRIOCEPTION/BALANCE EXERCISES**

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20R</td>
</tr>
<tr>
<td>2</td>
<td>20R</td>
</tr>
<tr>
<td>3</td>
<td>30s each leg</td>
</tr>
<tr>
<td>4</td>
<td>30s each leg</td>
</tr>
<tr>
<td>5</td>
<td>20R each leg</td>
</tr>
<tr>
<td>6</td>
<td>20R each leg</td>
</tr>
<tr>
<td>7</td>
<td>20R each leg</td>
</tr>
</tbody>
</table>

**STRETCHING**

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20R</td>
</tr>
<tr>
<td>2</td>
<td>20R</td>
</tr>
<tr>
<td>3</td>
<td>30s</td>
</tr>
<tr>
<td>4</td>
<td>30s</td>
</tr>
<tr>
<td>5</td>
<td>20R</td>
</tr>
<tr>
<td>6</td>
<td>20R</td>
</tr>
</tbody>
</table>

**AEROBIC TRAINING**

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>After 5 minutes</td>
</tr>
<tr>
<td>2</td>
<td>After 10 minutes</td>
</tr>
<tr>
<td>3</td>
<td>After 15 minutes</td>
</tr>
</tbody>
</table>

**STRENGTH TRAINING**

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>WITH ELASTIC BANDS</td>
</tr>
<tr>
<td>2</td>
<td>WITH BIG BALLS</td>
</tr>
<tr>
<td>3</td>
<td>WITH SMALL BALLS</td>
</tr>
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</table>

**SPPB**

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Walking</td>
</tr>
<tr>
<td>2</td>
<td>20R</td>
</tr>
<tr>
<td>3</td>
<td>20R</td>
</tr>
<tr>
<td>4</td>
<td>Top 2 steps</td>
</tr>
</tbody>
</table>

**FRIED Frailty Criteria**

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
</tr>
<tr>
<td>2</td>
<td>Exercise</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Basal</td>
</tr>
<tr>
<td>2</td>
<td>Post</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
</tr>
<tr>
<td>2</td>
<td>Exercise</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Basal</td>
</tr>
<tr>
<td>2</td>
<td>Post</td>
</tr>
</tbody>
</table>
Allogeneic Human Mesenchymal Stem Cell Infusions for Aging Frailty.
Revolution in Egypt
Joe Klein: What the U.S. should do
On the Street: Hope meets anxiety
Muslim Brotherhood: What it wants
Oscars: Portraits of star power

TIME
2045
The Year Man Becomes Immortal*
BY LEV GROSSMAN

Robotic Exoskeleton at Football World Cup - 2014
Juliano Pinto, 29-year-old male paraplegic, kicked the inaugural soccer ball wearing a robotic exoskeleton
Cap on head picked up signals from brain as he mentally visualized kicking the ball

Brazil
Inauguration of the Football World Cup
Corinthians Arena, Sao Paulo
Signals transmitted to the exoskeleton’s legs, which are moved by hydraulic forces

Developed by Walk Again Project, headed by Dr. Miguel Nicolelis of Duke University and a team of 150 researchers

PROPHETIC LETTER
Benjamin Franklin, in a 1780 letter to scientist Joseph Priestly said of the future:
“all diseases may by sure means be prevented or cured, not excepting that of old age, and our lives lengthened at pleasure even beyond the (current) standard...”
Clinical Practice Guidelines for the Management of Frailty

Strong Recommendations
1. We strongly recommend that frailty be identified using a validated measurement tool.
2. We strongly recommend that older adults with frailty be referred to a progressive, individualized physical activity program that contains a resistance training component.
3. We strongly recommend that polypharmacy be addressed by reducing or deprescribing any inappropriate/superfluous medications.

Conditional Recommendations
4. We conditionally recommend that persons with frailty are screened for causes of fatigue.
5. We conditionally recommend that older adults with frailty who exhibit unintentional weight loss should be screened for reversible causes and considered for food fortification/protein and caloric supplementation.
6. We conditionally recommend that vitamin D be prescribed for persons found to be deficient in Vitamin D.

No Recommendation
7. We have no recommendation for the provision of an individualized support and education plan for older adults with frailty.
P4 medicine in Sarcopenia:

P1 PREDICTIVE

Allelic Variations Associated with Strength and Body Mass

- Myostatin (GDF8, K133R)
- CNTF and its receptor
- Vitamin D receptor (VDR Bsm1)
- Angiotensin Converting Enzyme
- Androgen receptor gene (CAG-repeats)
- Cyclin dependent kinase inhibitor 1A
- MYOD1
- P53 – decreases satellite activation

HERTFORDSHIRE COHORT STUDY

SARCOPENIA ORIGINATES AT BIRTH

Sayer et al J Gerontol A 59:930,2004

GRIP STRENGTH CORRELATES WITH BIRTH WEIGHT

NOT INFANT GROWTH
Participants with a total score higher than 4 were classified as having sarcopenia.
The SARC-F Questionnaire: Diagnostic Overlap with Established Sarcopenia Definitions in Older German Men with Sarcopenia. Kemmler W¹, Sieber C, Freiberger E, von Stengel S.

<table>
<thead>
<tr>
<th>Variable</th>
<th>SARC-F:</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>without sarcopenia (n = 49)</td>
<td>with sarcopenia (n = 25)</td>
</tr>
<tr>
<td>Sarcopenia according to EWGSOP, %a</td>
<td>61</td>
<td>76</td>
</tr>
<tr>
<td>Sarcopenia according to IWGS, %b</td>
<td>35</td>
<td>80</td>
</tr>
<tr>
<td>Sarcopenia according to FNHI, %c</td>
<td>39</td>
<td>52</td>
</tr>
<tr>
<td>EWGSOP sarcopenia Z-score</td>
<td>-0.35±1.07</td>
<td>1.34±1.22</td>
</tr>
<tr>
<td>IWGS sarcopenia Z-score</td>
<td>0.35±1.74</td>
<td>2.07±1.77</td>
</tr>
<tr>
<td>FNHI sarcopenia Z-score</td>
<td>-0.19±2.23</td>
<td>1.37±2.08</td>
</tr>
<tr>
<td>Habitual gait velocity, m/s</td>
<td>1.03±0.21</td>
<td>0.83±0.13</td>
</tr>
<tr>
<td>Handgrip strength, N</td>
<td>27.1±5.2</td>
<td>23.6±4.3</td>
</tr>
<tr>
<td>SMI, kg/m²</td>
<td>6.99±0.36</td>
<td>6.89±0.62</td>
</tr>
<tr>
<td>SMI-FNHI, kg/BMI</td>
<td>0.783±0.115</td>
<td>0.764±0.95</td>
</tr>
</tbody>
</table>

- The lack of a unique mandatory definition or gold standard for sarcopenia complicates the reliable determination of the predictive power of the SARC-F.
- The diagnostic overlap between the SARC-F and presently applied sarcopenia consensus definitions was higher than among these definitions themselves.
- SARC-F can be used as a first simple screening method for sarcopenia.
SARC-F Results
7/1/2015 - 6/30/2017

<table>
<thead>
<tr>
<th>Category</th>
<th>No Sarcopenia</th>
<th>Sarcopenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician/Case Finding</td>
<td>60.6%</td>
<td>39.4%</td>
</tr>
<tr>
<td>Screening/Non-Physician</td>
<td>67.0%</td>
<td>33.0%</td>
</tr>
<tr>
<td>Nursing Home</td>
<td>18.6%</td>
<td>81.4%</td>
</tr>
<tr>
<td>PACE</td>
<td>34.1%</td>
<td>65.9%</td>
</tr>
</tbody>
</table>
P4 medicine in Sarcopenia

P3 PERSONALISED

- Resistance Exercise
- Leucine enriched essential amino acids or HMB
- Vitamin D
- Testosterone
- Myostatin peptobodies
## Perry County: Exercise Program

<table>
<thead>
<tr>
<th></th>
<th>Pre (41) mean</th>
<th>Range min-max</th>
<th>3m (41) Mean</th>
<th>Range Min-max</th>
<th>6m (31) Mean</th>
<th>Range Min-max</th>
<th>9m (25) mean</th>
<th>Range Min-max</th>
<th>12m (14) Mean</th>
<th>Range Min-max</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUG</td>
<td>15</td>
<td>47-8</td>
<td>12</td>
<td>30-6</td>
<td>13</td>
<td>28-7</td>
<td>12</td>
<td>21-7</td>
<td>13</td>
<td>26-8</td>
</tr>
<tr>
<td>FR</td>
<td>6</td>
<td>2-11</td>
<td>7</td>
<td>1-12</td>
<td>7</td>
<td>3-12</td>
<td>8</td>
<td>4-11</td>
<td>7</td>
<td>4-12</td>
</tr>
<tr>
<td>FTST</td>
<td>15</td>
<td>32-8</td>
<td>14</td>
<td>39-8</td>
<td>13</td>
<td>23-6</td>
<td>13</td>
<td>23-6</td>
<td>13</td>
<td>21-9</td>
</tr>
</tbody>
</table>

Measures high risk for falling, disability, and morbidity in older adults

- **TUG**: \( \geq 12 \) seconds
- **FR**: 6 inches or less
- **FTST**: \( > 13.6 \) seconds
PROVIDE (PROTEIN) STUDY CENTRES ACROSS EUROPE
P4 medicine in Sarcopenia: P4 PARTICIPATORY

Look Ahead - Diabetes

Compliance
Anorexia Independently Predicts Mortality

Hazard Ratio 2.9 (1.1-7.4)

Cornali et al JAGS 53 354, 2005

Cachexia Vs Protein Energy Malnutrition
Anorexia of Aging

↓ Smell

↓ Taste

↑ Leptin

↑ TNFα

↑ Choleystokinin

↓ Testosterone

↑ Fat Mass

Vagus

Opioids

NPY

↓ Nitric oxide

Decreased Food Intake
male > female

Adaptive Relaxation

Antral stretch occurs earlier

Decreased rate of gastric emptying

S.N.A.Q

1) My appetite is
   1. Very poor
   2. Poor
   3. Average
   4. Good
   5. Very good

2) When I eat, I feel full after
   1. Eating only a few mouthfuls
   2. Eating about a third of a plateful
   3. Eating over half a plateful
   4. Eating most of the food
   5. Hardly ever

3) Food tastes
   1. Very bad
   2. Bad
   3. Average
   4. Good
   5. Very good

4) Normally I eat
   1. Less than one full meal a day
   2. One meal a day
   3. Two meals a day
   4. Three meals a day
   5. More than three meals a day, including snacks

< 15 predicts significant weight loss within 6 months
SNAQ Results
7/1/2015 - 6/30/2017

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician/Case Finding</td>
<td>64.6%</td>
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<td>44.4%</td>
</tr>
<tr>
<td>PACE</td>
<td>59.1%</td>
<td>40.9%</td>
</tr>
</tbody>
</table>
Glasgow Prognostic Score

The GPS
  CRP ≥10 mg/l and albumin ≥35 g/l 0
  CRP >10 mg/l 1
  Albumin <35 g/l 1
  CRP >10 mg/l and albumin <35 g/l 2

The mGPS
  CRP ≤10 mg/l and albumin ≥35 g/l 0
  CRP >10 mg/l 1
  CRP >10 mg/l and albumin <35 g/l 2

CRP = C-reactive protein, GPS = Glasgow prognostic score, mGPS = Modified Glasgow prognostic score.
<table>
<thead>
<tr>
<th>M</th>
<th>Medication effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>Emotional problems, especially depression</td>
</tr>
<tr>
<td>A</td>
<td>Anemia, alcoholism</td>
</tr>
<tr>
<td>L</td>
<td>Late-life paranoia</td>
</tr>
<tr>
<td>S</td>
<td>Swallowing disorders</td>
</tr>
<tr>
<td>O</td>
<td>Oral factors (e.g., poorly fitting dentures, caries)</td>
</tr>
<tr>
<td>N</td>
<td>No money</td>
</tr>
<tr>
<td>W</td>
<td>Wandering and other dementia-related behaviors</td>
</tr>
<tr>
<td>H</td>
<td>Hyperthyroidism, hypothyroidism, hyperparathyroidism, hypoadrenalism</td>
</tr>
<tr>
<td>E</td>
<td>Enteric problems</td>
</tr>
<tr>
<td>E</td>
<td>Eating problems (e.g., inability to feed self)</td>
</tr>
<tr>
<td>L</td>
<td>Low-salt, low-cholesterol diet</td>
</tr>
<tr>
<td>S</td>
<td>Stones, social problems (e.g., social isolation, inability to obtain preferred foods)</td>
</tr>
</tbody>
</table>

ROMANA 3:
A phase 3 safety extension study of anamorelin in advanced non-small cell lung cancer (NSCLC) patients with cachexia.

Anamorelin versus placebo:

• significantly increased body weight from baseline of original trials at all time points ($P < 0.0001$)
• improved anorexia–cachexia symptoms at weeks 3, 6, 9, 12, and 16 ($P < 0.05$).
• No significant improvement in hand grip strength was seen in either group
MORTALITY RATE

0 %  20 %  40 %  60 %  80 %  100 %  120 %

200,000 BC  30,000 BC  1,000 BC  45 BC  1200 CE  1600 CE  1900 CE  1969 CE
The Palliative Care Trial Group Is Living *Longer* than the Usual Care Group (p NS)

<table>
<thead>
<tr>
<th></th>
<th>Palliative Care</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Days in Study</td>
<td>266 days</td>
<td>227 days</td>
</tr>
</tbody>
</table>
P4 medicine in DEMENTIA: P1 PREDICTIVE
Amyloid-B TAU Phosphorylation DECREASED MEMORY AMYLOID PLAQUES APOPTOSIS

Mitochondria OXIDATIVE DAMAGE

GSK-3 Overproduction Ch21 Presinilins/ApoE4 TAU Phosphorylation

AMYLOID PLAQUES EUROFIBRILLARY TANGLES

BAPtist THEORY

APP

ACh

LRF
Normal older persons have amyloid-beta plaques


- Clinical, pathological, and neurochemical changes in dementia: a subgroup with preserved mental status and numerous neocortical plaques.

- [Katzman R†, Terry R, DeTeresa R, Brown T, Davies P, Fuld P, Renbing X, Peck A.](https://doi.org/10.1001/archneur.1988.00470020090002) Postmortem examination was performed on 137 residents (average age 85.5 years) of a skilled nursing facility whose mental status, memory, and functional status had been evaluated during life.

- Ten subjects whose functional and cognitive performance was in the upper quintile of the nursing home residents, as good as or better than the performance of the upper quintile of residents without brain pathology (control subjects), showed the pathological features of mild Alzheimer's disease, with many neocortical plaques. Plaque counts were 80% of those of demented patients with Alzheimer's disease.

- The unexpected findings in these subjects were higher brain weights and greater number of neurons (greater than 90 micron 2 in a cross-sectional area in cerebral cortex) as compared to age-matched nursing home control subjects.
Seattle-based Adult Changes in Thought study

- Alzheimer’s disease ............ 45%
- Vascular based lesions ............. 33%
- Lewy Body Dementia ........... 10%

DEMENTIA is DECREASING in the United States
Diabetic Brain

- Depression
- Hypothyroidism
- Vitamin B12 deficiency
- Traumatic brain injury
- Inflammatory cytokines
- Falls
- Hypoglycaemia
- Oxidative damage
- Vascular lesions
- Leukoaraisis
- Atherosclerosis
- Arrhythmias, such as atrial fibrillation
- Cardiovascular autonomic dysfunctions
- Diabetic dementia

Metformin, Cognitive Dysfunction and Diabetics

OD in Diabetics Receiving Metformin
0.51 (0.22-0.99); P<.05

Long-term metformin usage and cognitive function among older adults with diabetes

Metformin use showed a significant inverse association with cognitive impairment in longitudinal analysis (OR = 0.49, 95% CI 0.29-0.85).

Dementia in Diabetes (VA)
11 year follow up, n=61010
HR for metformin 0.82
P4 medicine in Dementia: P2 PREVENTIVE

FINGER STUDY

Aged 60-77 years recruited from previous national surveys.
A 2 year multidomain intervention (diet, exercise, cognitive training, vascular risk monitoring), or a control group (general health advice).
1260 to the intervention group (n=631) or control group (n=629).

A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial
P4 medicine in Dementia:
P3 PERSONALIZED

- Drugs
- Emotional
- Metabolic
- Eyes and ears
- Normal Pressure Hydrocephalus
- Trauma
- Infection
- Atrial fibrillation/alcohol
- Sleep apnea

- Alzheimer disease
- Vascular Dementia
- Frontotemporal dementia
- Lewy-Body dementia
- Creutzfeld-Jaeger
- Primary Age Related TAUopathy
- Hippocampal Sclerosis
- Traumatic Brain Injury
- Diabetes related dementia
- ETC ETC ETC ETC
### Cognitive Deficit Reversal as Shown by Changes in the Veterans Affairs Saint Louis University Mental Status (SLUMS) Examination Scores 7.5 Years Later

<table>
<thead>
<tr>
<th></th>
<th>Correction of visual loss</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stability</td>
<td>1</td>
<td>[Reference]</td>
</tr>
<tr>
<td></td>
<td>Conversion</td>
<td>1.12 (0.27–4.71)</td>
<td>.877</td>
</tr>
<tr>
<td></td>
<td>Reversion</td>
<td>4.65 (1.58–13.70)</td>
<td>.005</td>
</tr>
</tbody>
</table>

#### Discontinuation of anticholinergic

|                          | Stability                 | 1 | [Reference] |
|                          | Conversion                | 1.88 (0.69–5.13) | .218 |
|                          | Reversion                 | 4.57 (1.87–11.18) | .001 |
P4 medicine in DEMENTIA:

- Medication Adherence
- Exercise
- Mediterranean Diet/Olive oil
- Don’t drive
- Attend with caregiver
- No guns
- Frequent toileting
- Socialisation
The Simple “FRAIL” Questionnaire Screening Tool
(3 or greater = frail; 1 or 2 = prefrail)

Fatigue: Are you fatigued?
Resistance: Cannot walk up one flight of stairs?
Aerobic: Cannot walk one block?
Illnesses: Do you have more than 5 illnesses?
Loss of weight: Have you lost more than 5% of your weight in the last 6 months?


SNAQ (Simplified Nutritional Assessment Questionnaire)
My appetite is
a. very poor
b. poor
c. average
d. good
e. very good

Food tastes
a. very bad
b. bad
c. average
d. good
e. very good

When I eat
a. I feel full after eating only a few mouthfuls
b. I feel full after eating about a third of a meal
c. I feel full after eating over half a meal
d. I feel full after eating most of the meal
e. I hardly ever feel full


Rapid Cognitive Screen (RCS)
1. Please remember these five objects. I will ask you what they are later. [Read each object to patient using approx. 1 second intervals.]

   Apple  Pen  Tie  House  Car

2. [Give patient pencil and the blank sheet with clock face.] This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o’clock. [2 pts/hr markers ok; 2 pts/time correct]
3. What were the five objects I asked you to remember? [1 pt/ea]
4. I’m going to tell you a story. Please listen carefully because afterwards, I’m going to ask you about it.

Jill was a very successful stockbroker. She made a lot of money on the stock market. She then met Jack, a devastatingly handsome man. She married him and had three children. They lived in Chicago. She then stopped work and stayed at home to bring up her children. When they were teenagers, she went back to work. She and Jack lived happily ever after.

What state did she live in? [1 pt]


Table I: SARC-F Screen for Sarcopenia

<table>
<thead>
<tr>
<th>Component</th>
<th>Question</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength</td>
<td>How much difficulty do you have in lifting and carrying 10 pounds?</td>
<td>None = 0</td>
</tr>
<tr>
<td></td>
<td>Some = 1</td>
<td>A lot or unable = 2</td>
</tr>
<tr>
<td>Resistance</td>
<td>How much difficulty do you have walking across a room?</td>
<td>None = 0</td>
</tr>
<tr>
<td></td>
<td>Some = 1</td>
<td>A lot, use aids, or unable = 2</td>
</tr>
<tr>
<td>Assistance</td>
<td>How much difficulty do you have transferring from a chair or bed?</td>
<td>None = 0</td>
</tr>
<tr>
<td></td>
<td>Some = 1</td>
<td>A lot or unable without help = 2</td>
</tr>
<tr>
<td>Rise from a chair</td>
<td>How much difficulty do you have climbing a flight of ten stairs?</td>
<td>None = 0</td>
</tr>
<tr>
<td></td>
<td>Some = 1</td>
<td>A lot or unable = 2</td>
</tr>
<tr>
<td>Climb stairs</td>
<td>How many times have you fallen in the last year?</td>
<td>None = 0</td>
</tr>
<tr>
<td></td>
<td>1-3 falls = 1</td>
<td>4 or more falls = 2</td>
</tr>
</tbody>
</table>

MISSOURI GATEWAY GWEP
Trained: 12,943
Screened: 6,037
Social Media: 104,368 / TV: 338703

Taiwan
China
Hong Kong
Singapore
New Zealand
Brazil
France

Cardinals Reminiscence League

Chicago (Rush)
Urbana-Champaign
Danville

Myrtle Hilliard Davis
Perry County Memorial Hospital

Complete Demonstration Programs

San Diego Alzheimer’s
National Training
Phoenix AMDA
Shelby County
Nashville
The 4 Ps of P4 Medicine

- Predictive
- Preventive
- Personalized
- Participatory
Sulfonylureas and Insulin increase mortality in diabetics; metformin doesn’t

Diabetics with autonomic neuropathy are at increased risk for sudden death. Need an implantable loop recorder?

Sleep apnea causes hypertension, hyperglycemia and cognitive dysfunction