

**Are Caregivers of a spouse with
Dementia
at Higher Risk for Cognitive
Decline/Dementia than
Non-Caregiver spouses ?**

*Peter. P. Vitaliano, Ph.D.
Psychiatry and Behavioral Sciences
University of Washington
Seattle, WA, USA*

Hypothesis

- Considers potentially *modifiable* risks for cognitive decline and/or dementia
- That *compromise* the ability of caregivers (CGs) to *function* in their roles
- Has *implications* for clinicians, researchers, policy makers, CGs and care recipients

Outline

- **Dementia/MCI -- Definitions and Risks**
- **CG Health as Risk for Dementia**
- **CG Cognitive Problems/Dementia**
- **Potential “Mediators” of CG Cognitive Problems/Dementia**
- **Problems with these “Mediators”**
- **Little to lose by mitigating “Mediators” - Suggestions**

Definitions

- ***Dementia*** Acquired reduction in cognitive abilities that interfere with daily function

Etiology Alzheimer's disease (AD), Vascular (VaD) and other dementias¹ diagnosed by clinical, historical, neuropsych, lab and imaging methods

- ***MCI*** Mild decline with minimal functional impairment – may be early detectable stages of dementia or may improve or remain stable over time²

Risks for Dementia/MCI

- **Age** Prevalence 3% between 65 - 74 yrs;
~ 50% for those 85 and older³
AD Incidence .08%/yr in persons 60-65
yrs old to 6.5%/yr in people 85+⁴
- **Education** AD risk decreases 17% each yr⁵
- **Apolipoprotein E (E4)** is consistent risk
factor for AD⁶ and MCI⁷
- **Family history**

OTHER “Potential” Risks for Cognitive Decline/*Dementia*

Psychosocial

Depression, Isolation

Behavioral

High Fat Diet, Sedentary

Physiological

Cortisol, Obesity, Insulin, Inflammation

Importantly

- * If Dementia is partially caused by exposures to environmental and behavioral Risk Factors, then spouses of persons with dementia were also exposed to these factors
- ** Many of these risks are associated with Chronic Stress which is higher in Spouse CGs than Spouse NCGs

PRE-CAREGIVING RISK FACTORS

Assortative Mating

Tendency to wed similar persons.¹⁹

Shared Life Style

Stressors, Distress, Behaviors as risks²⁰⁻²²

POST-CAREGIVING RISK FACTORS

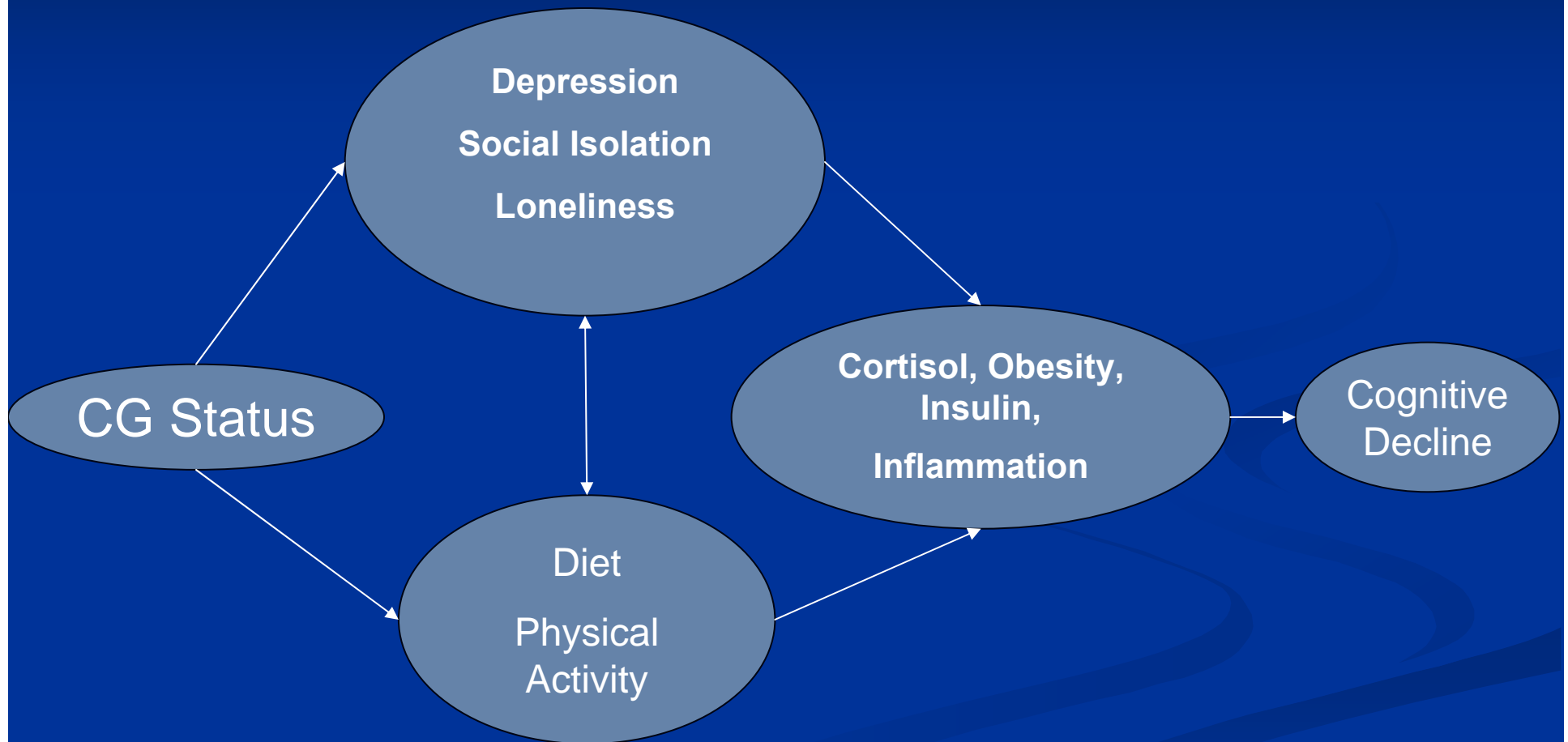
Chronic Stress

35 Hrs/ Wk of Care, more than any other CG

type¹⁰ Less Personal Time, Lost Work, Finances

Responses to Stress →

POST-CAREGIVING RISK FACTORS



Vitaliano (2010) *J American Geriatrics Society*

PSYCHOSOCIAL/BEHAVIORAL RISKS ASSOCIATED WITH COGNITIVE PROBLEMS/DEMENTIA

Social Isolation/Loneliness

Intellectually/socially disengaged lifestyle²⁵

Less cognitive stimulation (Use It or Lose It)²⁶

Depression

Predicts cognitive decline, MCI, dementia³¹⁻³⁴

Influences brain regions, promote decline³⁵

Poor Sleep

Deficits in cognitive function³⁷

Sedentary Behavior/Poor Diet

Exercise - lower incidence of cog decline/dementia⁴⁴⁻⁴⁶

Saturated/ trans fats may increase AD risk⁵¹⁻⁵²

Omega-3 may buffer cognitive decline⁵³

CAREGIVING AND PSYCHO-BEHAVIORAL RISKS

Social Isolation/Loneliness

Increases with care recipient's problems¹⁰

Greater risk for loneliness²³⁻²⁴

Depression/Sleep Problems

Greater Depression ($g = .58$)²⁸⁻²⁹

Mediates > Cog. Decline in CGs¹⁷

Poorer sleep quality³⁰

Sedentary Behavior/Poor Diet

Less physical activity³⁸⁻⁴¹

Greater daily calorie/fat intake⁴⁹

More likely to eat foods high in saturated fats⁵⁰

PHYSIOLOGIC RISKS FOR COGNITIVE/PROBLEMS

Cortisol

High chronic cortisol > memory impairment³⁵

< hippocampal volume/brain glucose metabolism⁵⁶

Obesity

Midlife Obesity predicts cognitive impairment^{65, 67}

Higher pro-inflammatory cytokines, insulin.

Inflammation

C-Reactive Protein increases risk of cog decline.⁸⁴

Men in the upper 3 CRP Qtiles have a 3X >

dementia risk than men in the lowest Qtile.⁸⁵

Hyper-Insulinemia (H-INS) and Cognition

- * AD risk is 2X > in older adults with **H-INS**
- * **H-INS** related to cog decline in persons without AD.⁷⁵
- * More cog problems in non-diabetic persons w/**H-INS**⁷¹⁻⁷²
- * Important to brain regions involved in learning/memory⁷⁰
- * If increase insulin levels to those of persons with IR, such persons show brain inflammation.⁷⁴

CAREGIVING AND PHYSIOLOGICAL RISKS

Cortisol

Chronic stress → excessive unremitting cortisol secretion
→ exhaustion → physical/ mental problems⁵⁵

Meta-Analysis (N = 3014): Stress Hormones and CG status
(r = .23); highest r of 11 health categories⁹

Obesity

CGs > weight gain, waist size, and obesity than NCGs^{50, 60,64}

Two studies: CGs > wt gain or obesity than NCGs⁶⁰⁻⁶¹

Hyperinsulinemia

Two studies show CGs > fasting insulin levels than NCGs^{61,69}

Inflammation

CGs > NCGs on: Increases (4X) in IL-6 levels over 6 years;⁸¹
Increases in CRP over 2 yrs, = at baseline.⁸²
Plasma D-dimer (thrombotic) levels.⁸³

TWO STUDIES OF CGS & NCGS

Variable	Study 1 (1989-95)		Study 2 (2000-05)	
N	CGs	NCGs	CGs	NCGs
	82	88	123	117
Age (mean yrs)	69.8 (7.9)	68.7(5.8)	71.4 (8.9)	70.2 (7.3)
Gender (% Women)	63	70	61	64
Race (% White)	100	100	94	93

PHYSIOLOGIC MARKERS

Variable	Study 1		Study 2	
	CGS 82	NCGS 88	CGS 123	NCGS 117
HTN1 (Time 1)	53	49	71	64
HTN2 (Time 2)	49	40	75	67
Lipidemia1	39	36	48	40
Lipidemia2	38	40	46	38
H-Glycemia1	13	10	21	14
H-Glycemia2	20	17	18	14
H-Insulinemia1	50	36*	50	36*
H-Insulinemia2	56	42*	57	43*
Obesity1	20	10**	29	16*
Obesity2	29	10**	29	16*

Given that :

- 1) CGs have Shared a life with someone who develops dementia, and they have**
- 2) Greater risks for Cognitive Problems, and**
- 3) Chronic Stress can impair Cognitive Function**

Is there evidence that CGs are at higher risk for cognitive problems/dementia?



Only 7 independent studies

have compared

Cognition/Dementia Rates

in CGs vs. NCGs

STUDY 1

Caswell LW, Vitaliano PP, et al. 2003.

Age = 71 yrs, 15 yrs Ed, 61% Women

44 Spouse CGs lower *Digit Symbol Test (DST)*
than 77 Spouse NCGs

Vitaliano PP, Echeverria D, et al. 2005

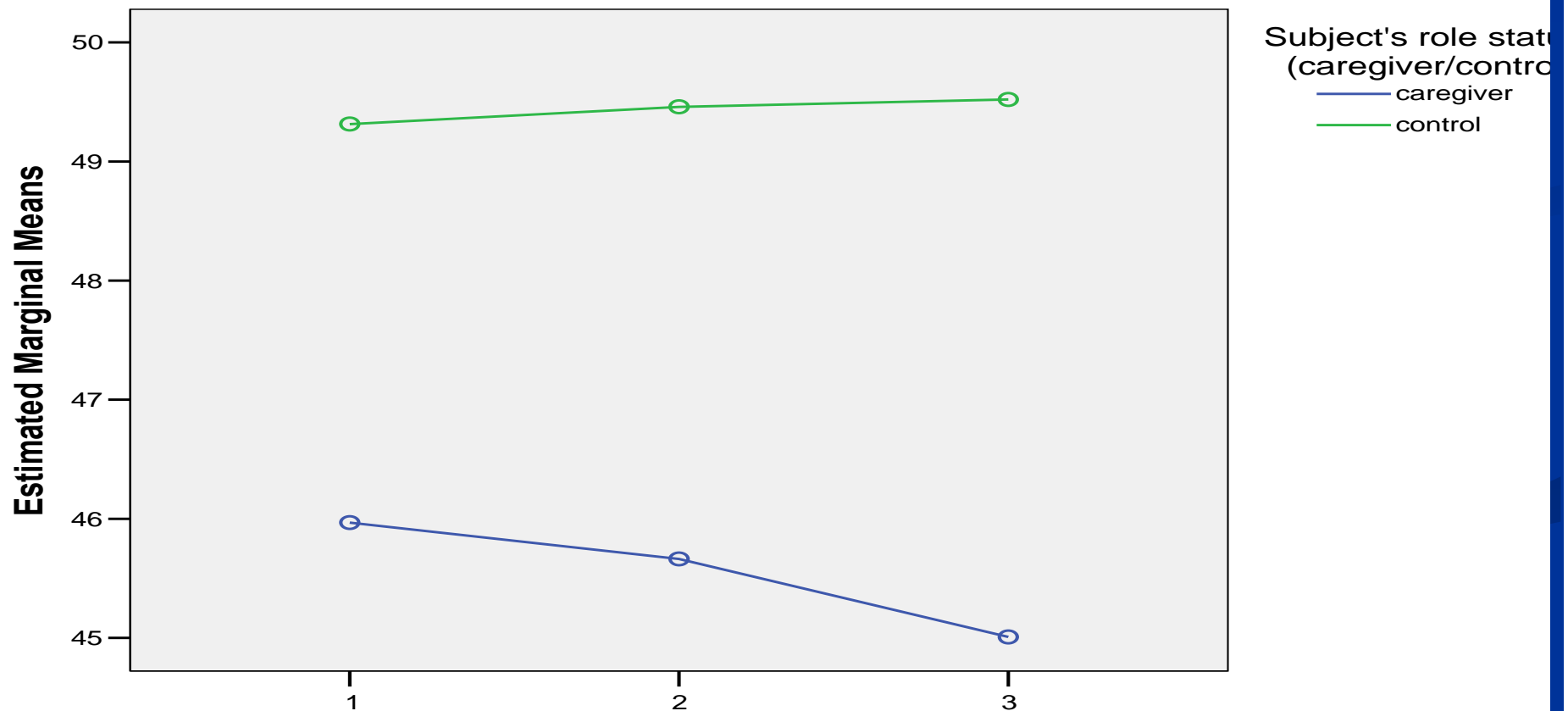
98 spouse CGs had 2 year decline in *Shipley Vocabulary*
vs no decline in 96 spouse NCGs. *Mediated by higher
Insulin and Obesity in CGs than NCGs*

Vitaliano PP, Zhang, et al. 2009

122 spouse CGs had 2 year decline on *DST* vs. no decline
in 117 spouse NCGs. *Mediated by higher Depression in
CGs than NCGs.*

Digit Symbol Test Scores for CGs and NCGs over two years

Estimated Marginal Means of MEASURE_1



STUDY 2

Mackenzie CS, Smith MC, Hasher L, Goldstein D, et al. 2007.

Age = 79 yrs, 70% women

27 CGs providing palliative care poorer than norms for *Episodic Memory, Working Memory, Attention*

STUDY 3

MacKenzie CS, Wiprzycka UJ, Hasher L, et al. 2009

Age = 79 yrs, 70% women

16 spouse CGs poorer *Learning, Episodic Recall after short/long delays, Working Memory* than 16 spouse NCGs

STUDY 4

Lee S, Kawachi I et al, 2004

13,740 Nurses' Health Study (all women)

Aged 70-79 yrs, Telephone-administered

CGs poorer than NCGs on *Immediate/Delayed Recall, Verbal Fluency, Digit Span Backwards*

STUDY 5

de Vugt ME, Jolles J, van Osch L, et al. 2006

54 CGs and 108 NCGs; Age = 68 yrs, 59% Women

CGs poorer than NCGs on *Global Mental Status, Delayed Recall and DST*

STUDY 6

Haley W., Roth, D., Howard, G. et al, 2010.

716 CGs; Framingham Stroke Risk Score
(projected 10-yr risk of incident stroke)

23% higher adjusted *Stroke Risk*

(13.6% for high-strain vs. 11% for no strain CGs).

STUDY 7

Norton MC, Smith, KR, Østbye, T et al. 2010

Followed 1,221 married couples aged ≥ 65 yrs

Over 12 yrs, Spouses of persons who
developed dementia had a 6X greater
dementia risk than spouses of persons with
no dementia (12X for men, 4X for women).

Consequences of Poor Caregiver Cognition

■ *Short Term*

Difficulties Managing Household Tasks, Family responsibilities, Finances & Legal decisions

Difficulties Coordinating Schedules,
Remembering Appointments,
Managing Medications

■ *Long Term*

Caregiver Illness and then downward spiral in both parties.

Cognitive Problems predict Functional Problems

OVER TWO YEARS, FUNCTIONAL IMPAIRMENT INCREASES 85% FASTER IN 123 CGs THAN 117 NCGs. THIS IS EXPLAINED BY PSYCHOSOCIAL, PHYSIOLOGICAL AND COGNITIVE FUNCTION

Vitaliano, Echeverria, Young et al (2007)⁸²

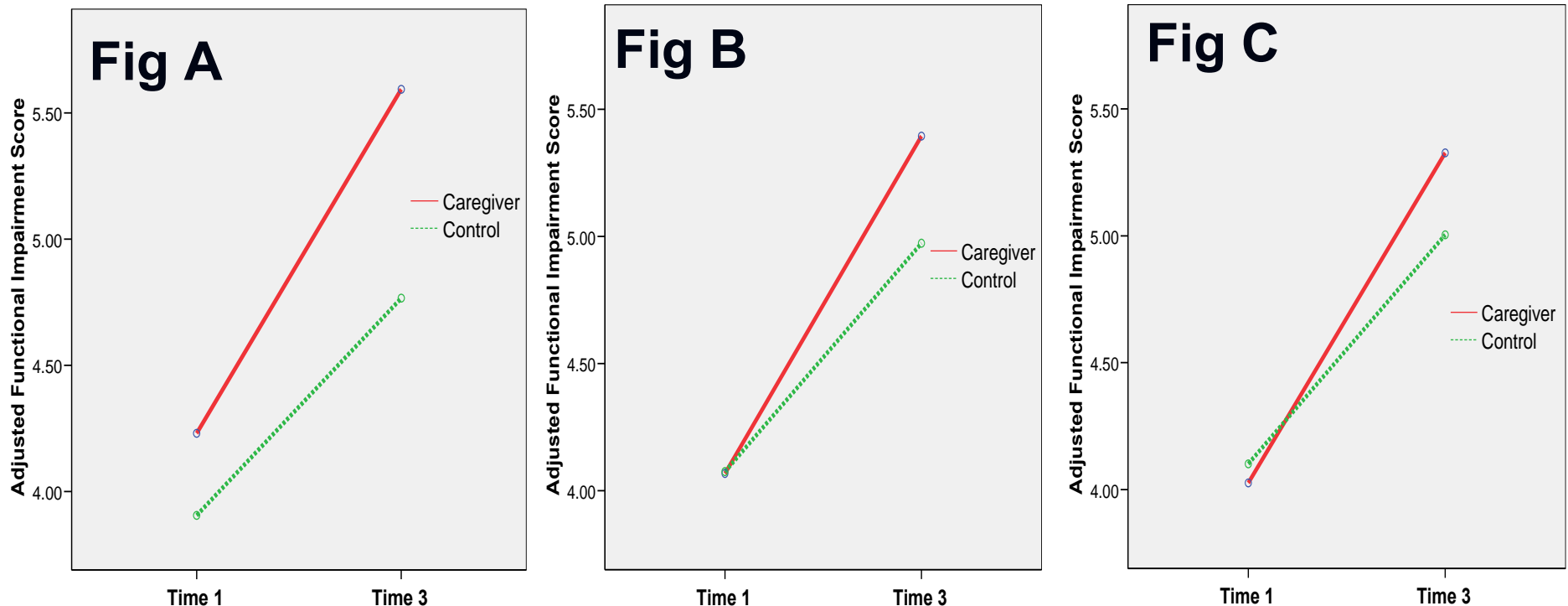


Figure A controlling for coronary procedures, anti-hypertensive medications, psychotropic medications, weekly intake of hard liquor, and BMI.

Figure B controlling for covariates in A, C-reactive protein change(YR3 –YR1), CRP and Psychological Distress at T1.

Figure C controlling for covariates in A & B and DST at T1 and DST (YR2-YR1).

Problems with these “Mediators”

- 1.** Even if a factor repeatedly predicts cognitive decline/dementia, it may not be a *sufficient condition for causality* because it may be a *preclinical effect of early dementia*.
- 2.** The causes of cognitive decline/dementia are *likely multivariate, non-linear* and probably have *interacting feedback* loops that exacerbate their influence on cognition; some may occur prior to, and others in the context of, caregiving over time.
- 3.** Only way to establish ‘causal relationship’ is via an RCT where CGs are randomized and mediator is examined as part of treatment vs. no treatment, with cognition as outcome.

Problems with these “Mediators”

4. Plassman et al (2010) reviewed 127 observational studies and 22 RCTs of risk/protective factors of cognitive decline (1984-2009).

Few Studies had sufficient evidence to firmly conclude associations with cognitive decline.

***Likely Associated:* Diabetes, Depression, MetS.**

***Probably Associated:* Cognitive, Physical, Leisure Activities/Dietary Factors, often CIs ~ 1.0.**

Only one quality cognitive training RCT (i.e., memory, reasoning, processing speed) and one physical exercise RCT had cognitive benefits.

THE JURY MAY STILL BE OUT ON THE RISK AND PROTECTIVE VALUE OF SEVERAL OF THESE PSYCHOSOCIAL, BEHAVIORAL AND PHYSIOLOGICAL FACTORS, BUT WE HAVE LITTLE TO LOSE BY ASSUMING THEY ARE RELEVANT TO FUTURE DEMENTIA

WHY?

**WHAT IS GOOD FOR THE HEART SHOULD BE GOOD FOR THE BRAIN
DIET, EXERCISE, POSITIVE MOOD ARE ALL
“PROVEN” TO PREVENT CV Illnesses**

Caregiver Tools Fortunately, many putative risk factors for cognitive problems are amenable to change.

- I. Pleasant Events (D. Gallagher). CG Life Satisfaction - Identify, monitor, reinforce Positive Mood. Reduces depression in CGs, should also help with cognition.
- II. Exercise (A. King) RCT of moderate to intense exercise reduced CG stress-induced CV Reactivity and improved sleep quality in CGs ⁴² Influence cognition? New research (L. Baker) promising, but may be too much exercise commitment for CGs (serious problem).
- III. Nutrition During National Nutrition Month, Strength for Caring (www.StrengthforCaring.com), resource for CGs, provides healthy recipes and food charts.
- IV. Cognitive Training (ACTIVE) RCT shown to maintain cog function in older adults, but may be too intensive for CGs.

CG Cognition and Society

- Beyond the expected effects on the QOL and health of CGs, declines in CG cognition and function should have substantial costs to society.
- Total direct costs of care for persons with AD living at home are 21% lower than for comparable persons living in an institution.¹⁰⁷
- CGs provide > 80% of long-term care services, 8.5 billion hrs/year to persons with AD, valued at \$94 B annually using minimum wage calculations¹⁰⁵. Figure greatly exceeds national spending for home health/nursing home care.¹⁰⁶



Sample Combinations	Spouse	CG	Dementia
CGs of Spouse with Dementia	1	1	1
Spouse CGs of other Dx's (e.g. cancer)	1	1	0
Spouse NGs of persons w/Dementia	1	0	1
Spouses who are neither CGs or have spouse with dementia	1	0	0
Non-spouse CGs of persons w/dementia (daughters)	0	1	1
Non-spouse CGs of persons with other Dx	0	1	0