ACETYL-L-CARNITINE SUPPLEMENTATION FOR THE TREATMENT FOR DEPRESSIVE SYMPTOMS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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CONFLICT OF INTEREST DISCLOSURE

I have no potential conflict of interest to report

INTRODUCTION

- Depression is common and affects about 350 million people worldwide and was **the second leading cause** of global disability.
- **Alterations of fatty acids and lipid metabolism**, important contributors of neuroplasticity, often occur in depressed persons.
- **Carnitine** appears to modulate the activity of several neurotrophic factors, cell membranes, lipid metabolism, and neurotransmitters in nervous tissues.

ROLE OF ALC IN DEPRESSION
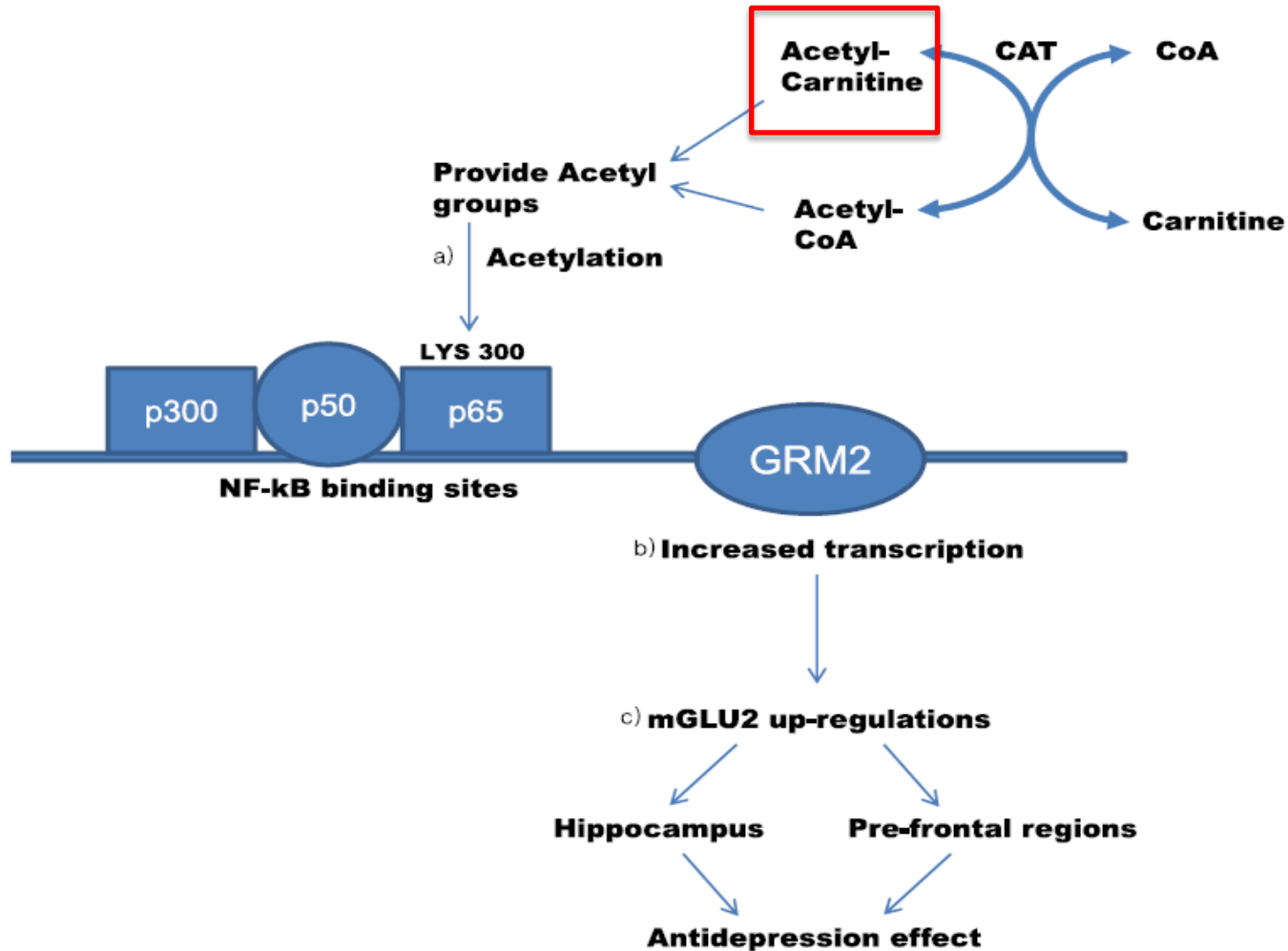
Wang SM et al. J of Psych Res, 2014: 30e37.

AIMS

•A recent narrative review reported that ALC may be potentially effective and tolerable option for people affected by depression, in particular who are **vulnerable** to **adverse events** from antidepressants, such as **older people**.

•To summarize the current evidence regarding the use of ALC as anti-depressant agent

- ▪ **compared to placebo (**or no intervention**)**
- ▪ compared to **common antidepressant agents**.

METHODS

- **Search strategy (until end 2016)**

1. **RCTs, ALC, depressive symptoms.**

2. **Several databases.**

3. **Full texts/conference abstracts, any language.**

- **Inclusion/exclusion criteria**

Inclusion	Exclusion
RCTs	Observational
ALC (also as add-on)	Not validated scales for depression
Reporting data on depressive symptoms	No data regarding depression

- **Outcomes/statistical analysis**

1. **SMDs→** changes of depressive symptoms in ALC vs. controls.

2. **Random-effect model→**I2>50%→meta-regression/sensitivity analyses.

3. **Publication bias.**

RESULTS (1): PRISMA
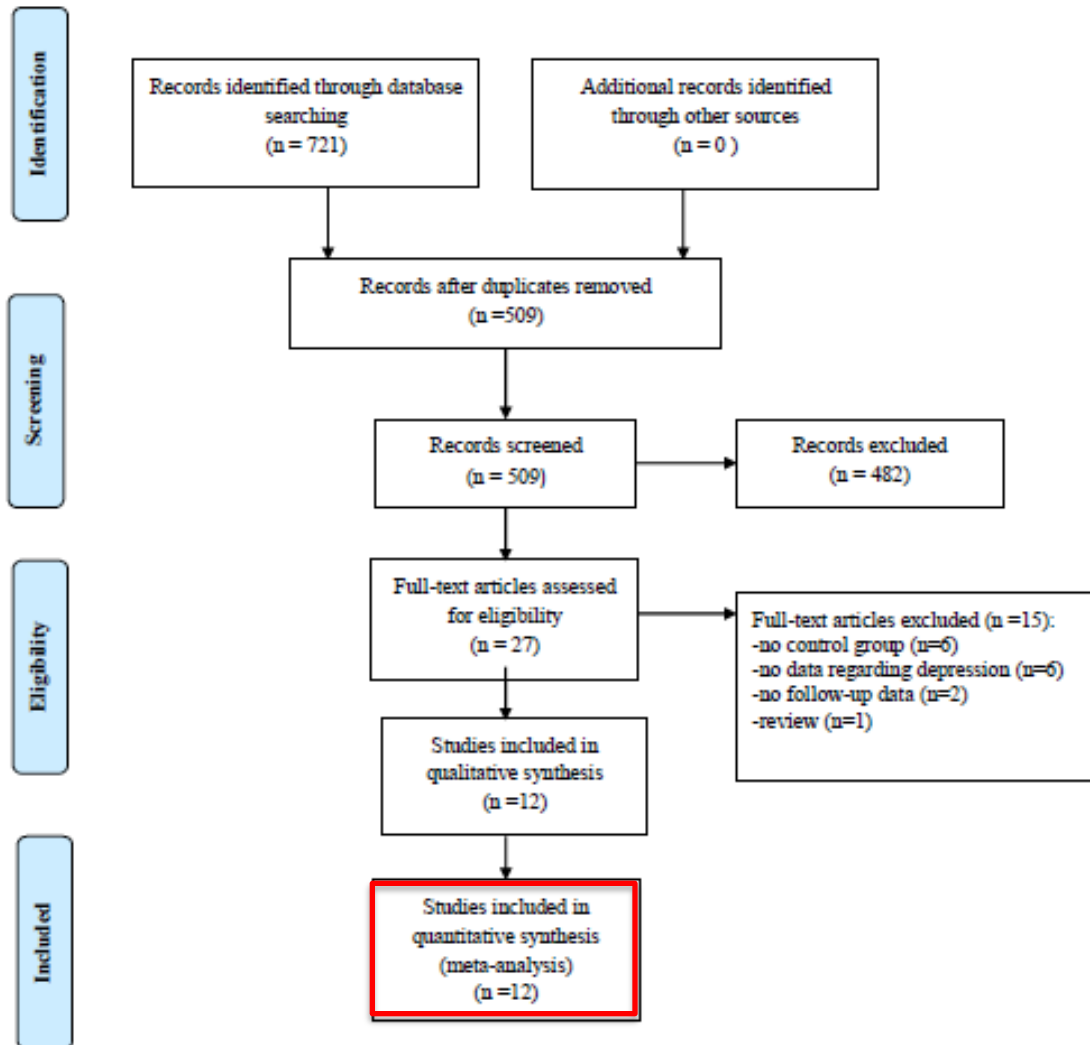
RESULTS (2): PLC/NONE

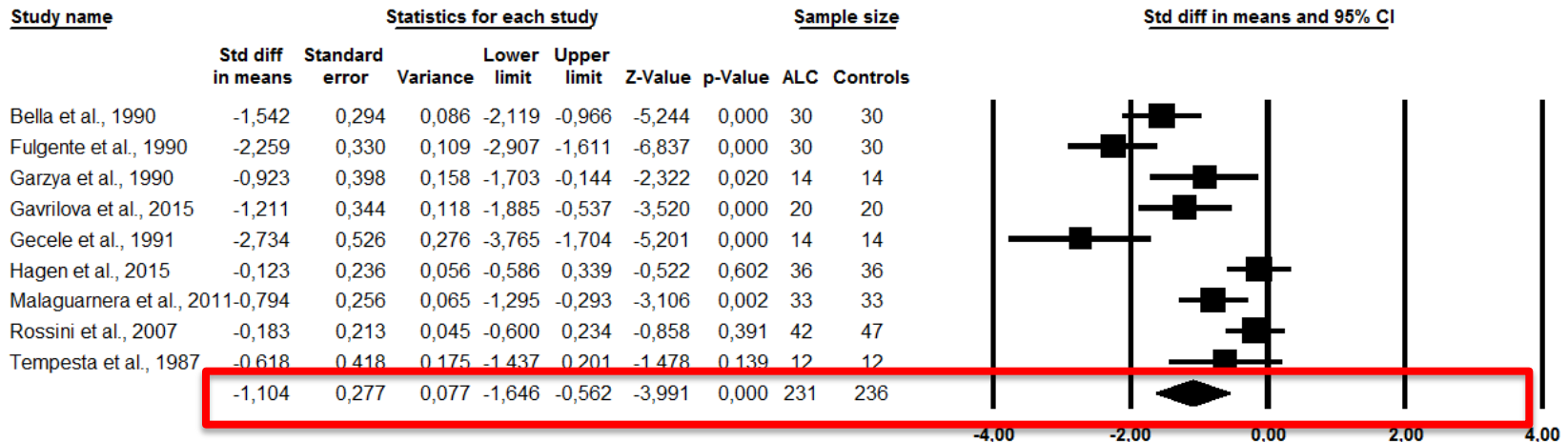## Nine RCTs, 231 ALC vs. 236 controls; follow-up: 8 weeks

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	ALC	Controls
Bella et al., 1990	-1,542	0,294	0,086	-2,119	-0,966	-5,244	0,000	30	30
Fulgente et al., 1990	-2,259	0,330	0,109	-2,907	-1,611	-6,837	0,000	30	30
Garzya et al., 1990	-0,923	0,398	0,158	-1,703	-0,144	-2,322	0,020	14	14
Gavrilova et al., 2015	-1,211	0,344	0,118	-1,885	-0,537	-3,520	0,000	20	20
Gecele et al., 1991	-2,734	0,526	0,276	-3,765	-1,704	-5,201	0,000	14	14
Hagen et al., 2015	-0,123	0,236	0,056	-0,586	0,339	-0,522	0,602	36	36
Malaguarnera et al., 2011	-0,794	0,256	0,065	-1,295	-0,293	-3,106	0,002	33	33
Rossini et al., 2007	-0,183	0,213	0,045	-0,600	0,234	-0,858	0,391	42	47
Tempesta et al., 1987	-0,618	0,418	0,175	-1,437	0,201	-1,478	0,139	12	12
	-1,104	0,277	0,077	-1,646	-0,562	-3,991	0,000	231	236

ALC Controls

RESULTS (2): AGE

Group by age	Study name	Std diff in means	Standard error	Lower limit	Upper limit	p-Value
older	Bella et al., 1990	-1,542	0,294	-2,119	-0,966	0,000
older	Fulgente et al., 1990	-2,259	0,330	-2,907	-1,611	0,000
older	Garzya et al., 1990	-0,923	0,398	-1,703	-0,144	0,020
older	Gavrilova et al., 2015	-1,211	0,344	-1,885	-0,537	0,000
older	Gecele et al., 1991	-2,734	0,526	-3,765	-1,704	0,000
older	Tempesta et al., 1987	-0,618	0,418	-1,437	0,201	0,139
older		-1,524	0,290	-2,093	-0,955	0,000
younger	Hagen et al., 2015	-0,123	0,236	-0,586	0,339	0,602
younger	Malaguarnera et al., 2011	-0,794	0,256	-1,295	-0,293	0,002
younger	Rossini et al., 2007	-0,183	0,213	-0,600	0,234	0,391
younger		-0,351	0,204	-0,751	0,049	0,085

Statistics for each study

Std diff in means and 95% CI

ALC   Controls
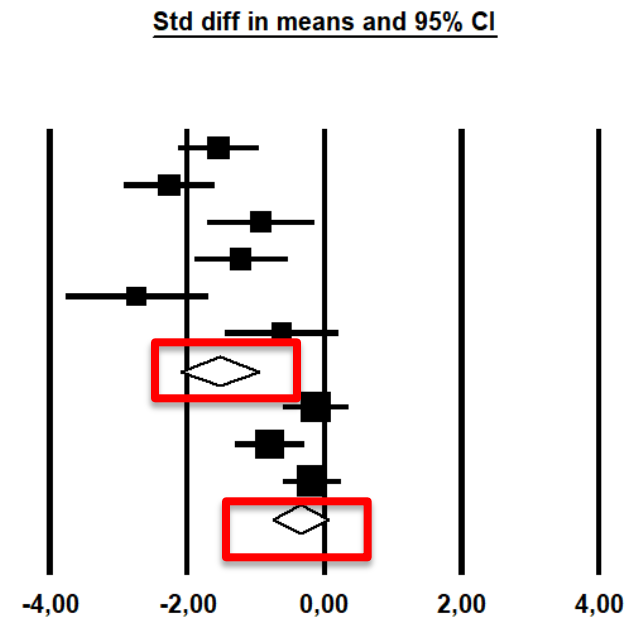
Veronese et al., Psych Med., 2017, in press

RESULTS (3): ANTIDEPR

Three RCTs, 162 ALC vs. 162 controls; follow-up: 12 weeks

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	ALC	Antidepressant
Bersani et al., 2013	-0,238	0,224	0,050	-0,678	0,202	-1,061	0,289	41	39
Leombruni et al., 2015	0,346	0,285	0,081	-0,213	0,904	1,214	0,225	22	29
Zanardi et al., 2006	0,114	0,144	0,021	-0,168	0,397	0,792	0,429	99	94
	0,058	0,144	0,021	-0,224	0,340	0,405	0,686	162	162

Std diff in means and 95% CI

-4,00   -2,00   0,00   2,00   4,00

ALC   Antidepressant

RESULTS (4): ADVERSE EVENTS

Study name	Statistics for each study							Risk ratio and 95% CI
	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	ALC	Controls	
Bersani et al., 2013	0,370	0,174	0,787	-2,582	0,010	7 / 41	18 / 39	
Leombruni et al., 2015	0,077	0,005	1,262	-1,797	0,072	0 / 22	8 / 29	
Zanardi et al., 2006	0,356	0,224	0,565	-4,377	0,000	18 / 99	48 / 94	
	0,349	0,236	0,516	-5,282	0,000	25 / 162	74 / 162	

ALC   Controls
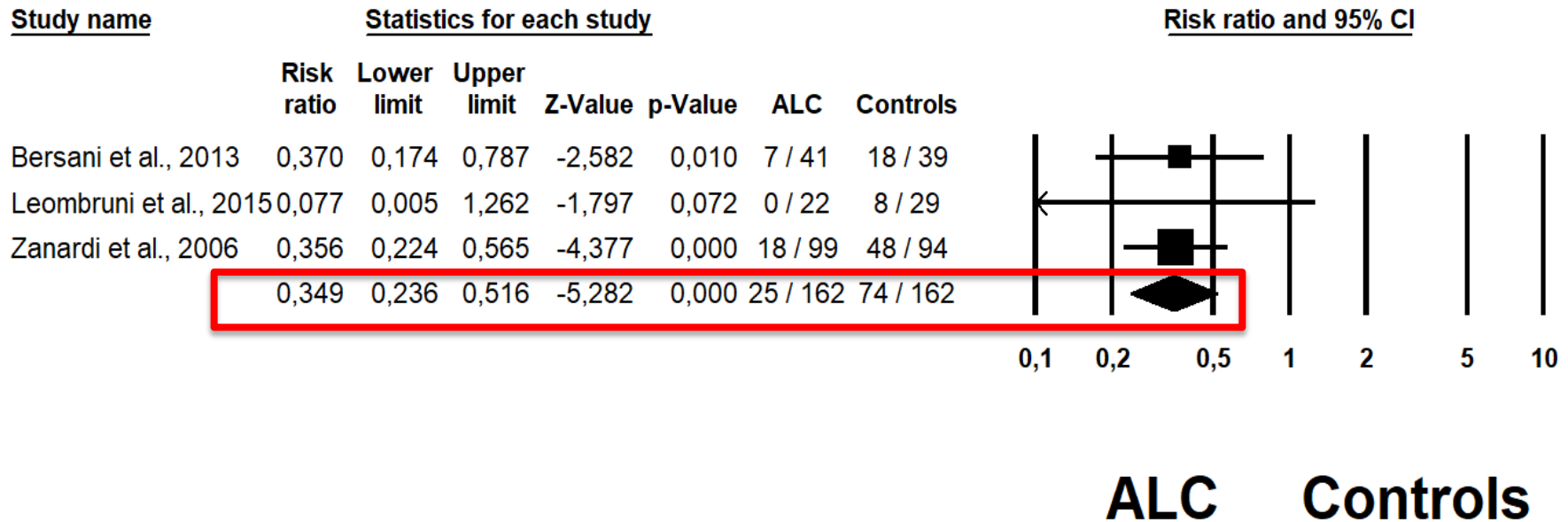
Veronese et al., Psych Med., 2017, in press

CONCLUSIONS

- ALC supplementation appears to confer a **significant decrease in depressive symptoms** compared to placebo/no intervention.

- ALC appears to have a **similar effect to some common antidepressant agents** with significantly fewer side effects.

- The use of ALC is **safer than some traditional antidepressants** suggesting a potential role of ALC for treating depression in older people .