Supplementary Material

Article Title: Adherence to Antidepressants Is Associated With Lower Mortality: A 4-Year Population-Based Cohort Study

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List of Supplementary Material for the article

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Supplementary Table 1: Previous studies examining the association between antidepressants use and all-cause mortality

[a] HR for Selective Serotonin Reuptake Inhibitors:1.26 and for Other AD:1.67

[b] HR 1.22 for AD use and no dep., HR 2.97 for AD use with dep. compared to no AD use and no dep.

[c] HR For tricyclic antidepressant:0.5 and for Other AD:0.66

[d] Risk ratio for mortality of AD users vs. AD non users during 1 year.

Study	N	Sample	Country	variable	Maximal follow-up period	Covariates	HR for mortality
Scherrer et al. [33]	4,037	Post-MI & Dep.	USA	<12 wk. AD	7 yrs	SDV, Anxiety, HSU	0.33
Gallo et al. [35]	1,226	age>60 yrs & Dep.	USA	AD use vs. none	5 yrs	SDV, SmS, CCI, cognition, and suicidal ideation	0.67
Tiihonen et al. [26]	15,390	Hospitalized suicide attempters	Finland	AD use vs. none	7 yrs	SDV, no. of previous AD prescriptions, and no. of previous suicide attempts	0.64

Study	N	Population	Country	Comparison	Follow-up	Adjustments	Result
Berkman et al. [34]	2,481	Post-MI & Dep.	USA	AD use vs. none	5 yrs	Age, baseline BDI score, Killip class, ejection fraction, creatinine level, previous MI, prior medical diagnoses	NS
Glassman et al. [39]	361	Acute coronary syndrome & Dep.	USA	AD use vs. none	7 yrs	Age, gender	0.42
Coupland et al. [24]	60,746	age>65 yrs & Dep.	UK	AD class use vs. none	12 yrs	SDV, previous dep., severity of index Dep., deprivation, SmS, comorbidities, use of other drugs and previous falls	1.16-1.67[a]
Almeida et al. [36]	5,276	68-88 yrs, men +/- Dep.	Australia	AD use -/+ dep. vs. no AD no dep.	7 yrs	age, education, migrant status, physical activity, SmS, alcohol use and CCI	1.22-2.97[b]
Ryan et al. [37]	7,363	Elderly	France	AD use vs. none	4 yr	SDV, cognition, alcohol consumption, SmS, disability, recent hospitalization, comorbidity, weight	2.22
Scherrer et al. [40]	93,653	Dep. w/o cardiac disease	USA	AD class 12 wk. use vs. less	7 yrs	SDV, Anxiety, Cardio-vascular indices, Dep. severity	0.5-0.66[c]
Bingefors et al. [41]	456	AD	Sweden	AD use vs. none	9 yrs	SDV, physical diseases	1.52

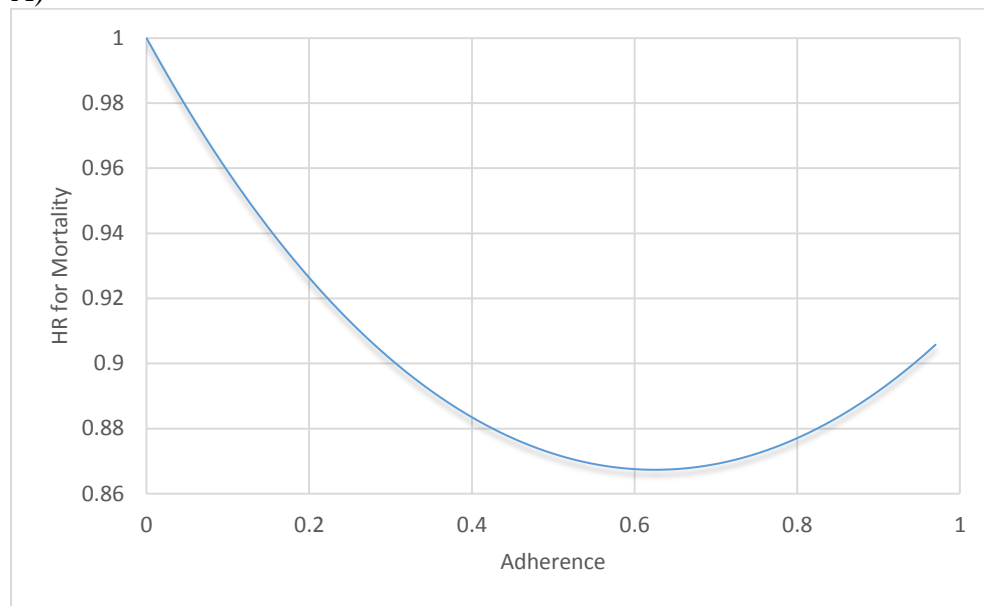|	AD vs. 912 MC	prescribed vs. MC					
Sundell et al. [25]	94,239	Age 20-34	Sweden	AD use vs. none	1 yr	Gender	4.39[d]

MI – Myocardial Infarction. Dep. – Depression, AD – Antidepressants, wk – Week, SDV – Socio-Demographic Variables,

HSU – Health Service Utilization, SmS - Smoking Status, CCI – Charlson Comorbidity Index, MC – Matched control,

HR – Hazard ratio, NS- Non Significant
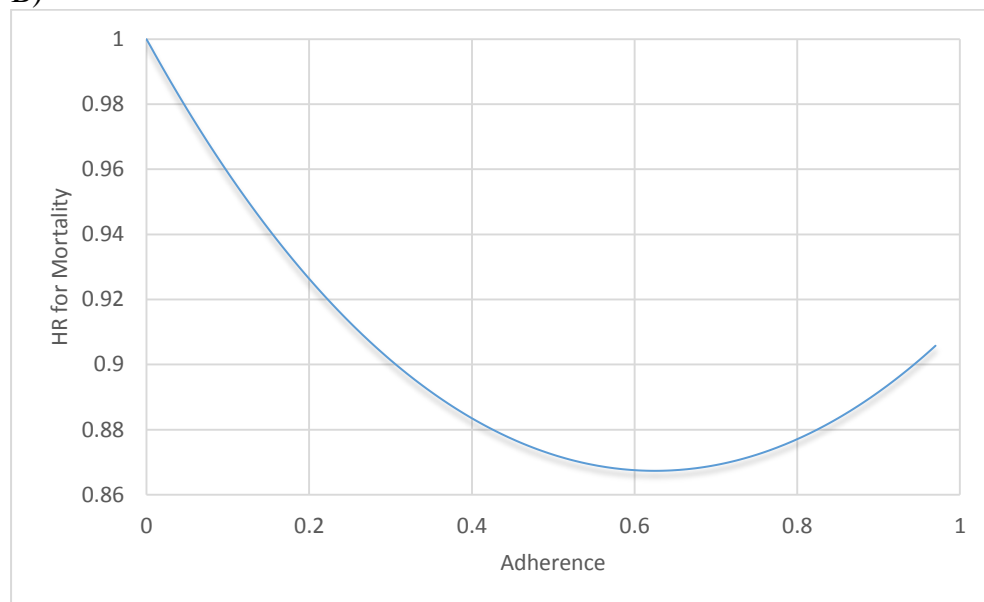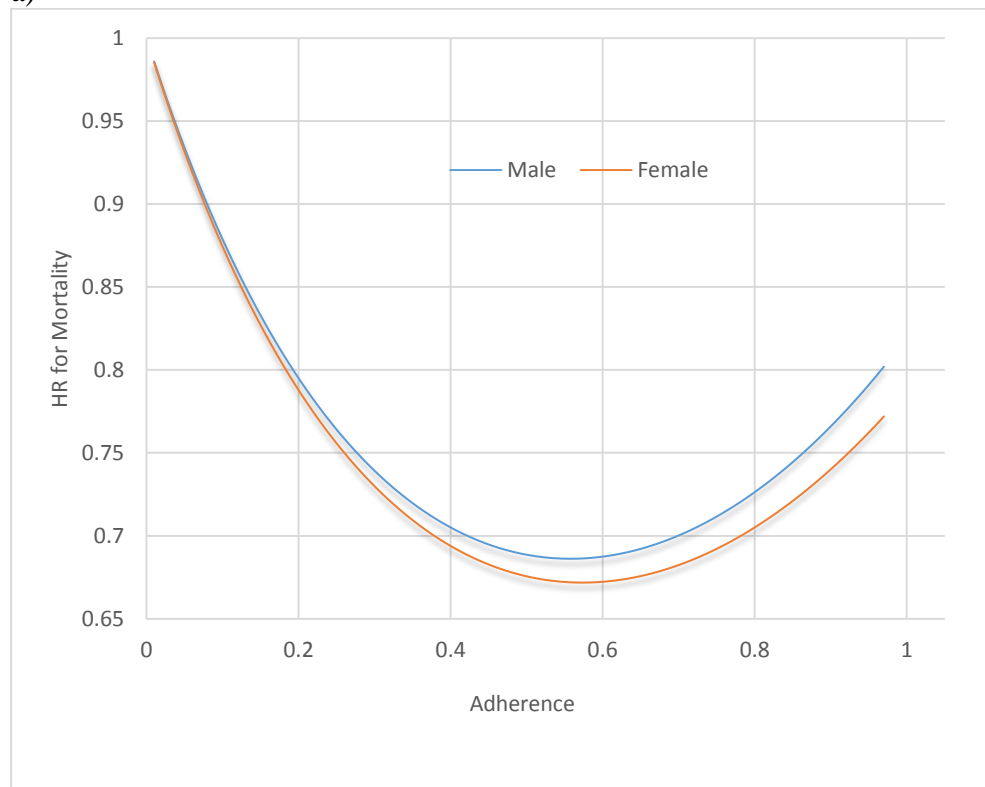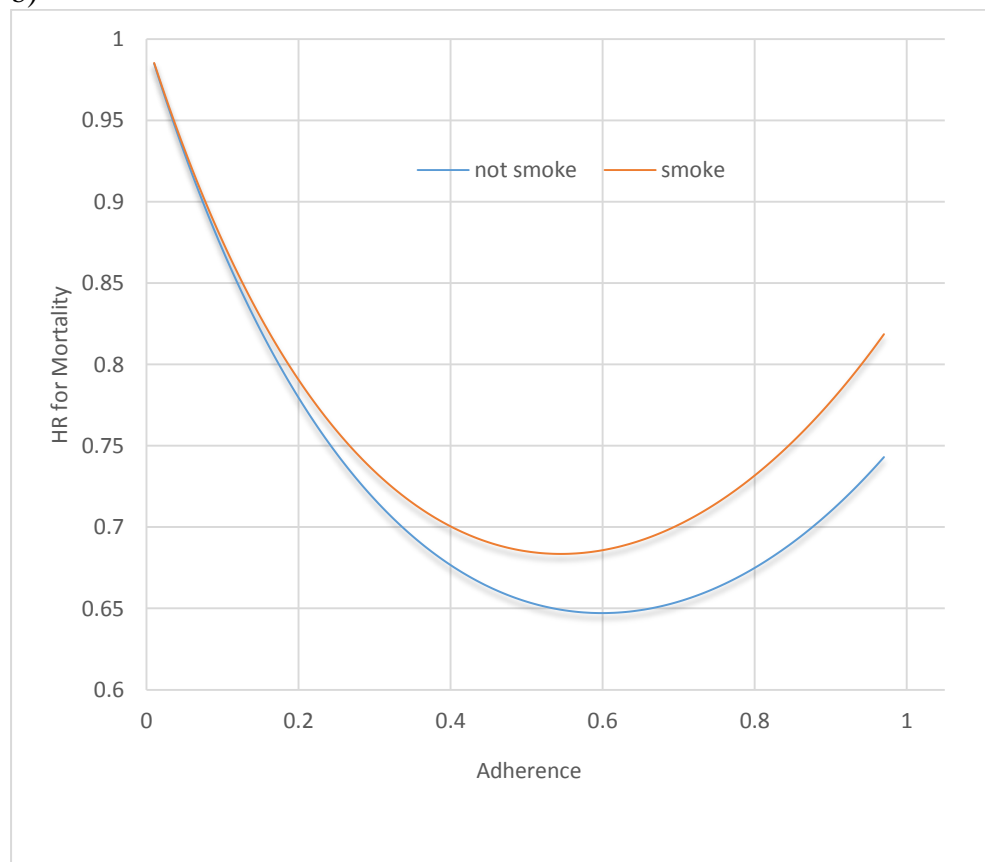
Supplementary figure 1:
A)

B)

Figure 1: Polynomial regression model of mortality hazard by continuous adherence level, adjusted for age, gender, smoking status, socioeconomic status and Charlson comorbidity score: a) population with follow-up time of three months or more (n=236,262). b) Population with follow-up time of 18 months or more (n=166,812).

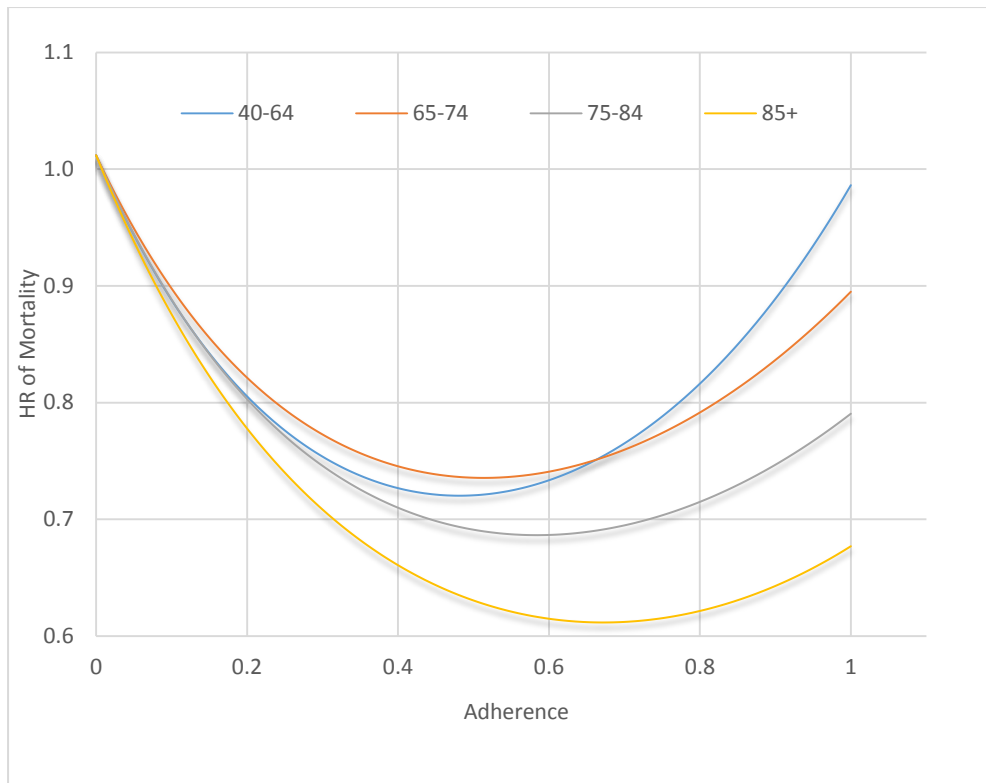Supplementary Figure 2 –
a)

b)

c)

Figure 2S: Polynomial regression model of mortality hazard by continuous adherence level across: a) gender b) smoking status c) age group
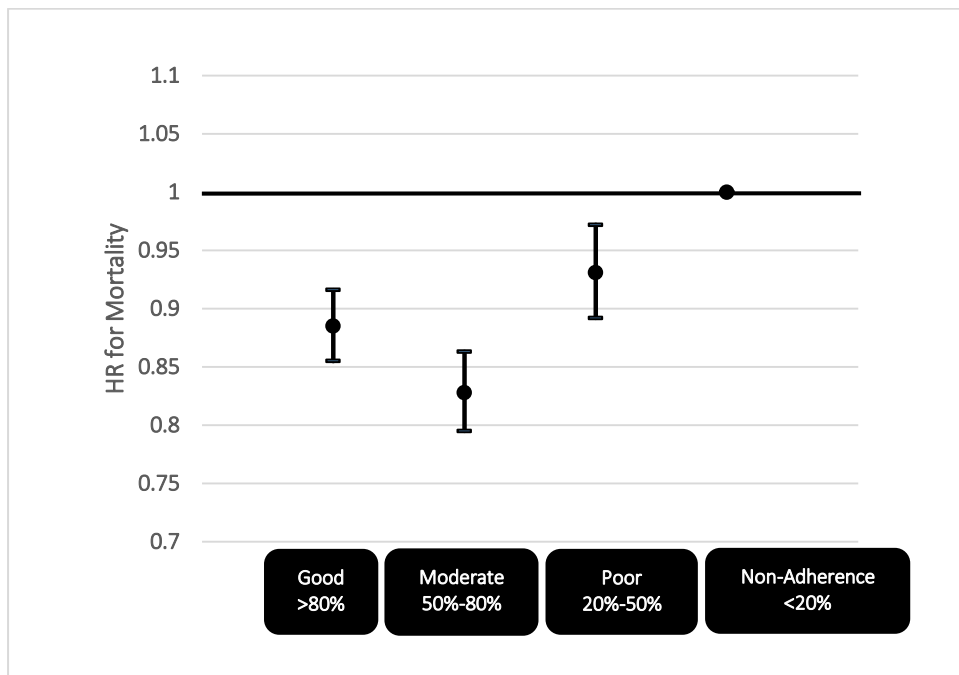
Supplementary figure 3

Figure 3s: Relative hazard ratios (HR) for mortality and 95% confidence intervals across clustered adherence levels during 4 years follow-up (N=251,745). Non adherence level (<20%) serves as the reference. Adjusted for sex, age, smoking status, socio-economic status and Charlson's comorbidity score
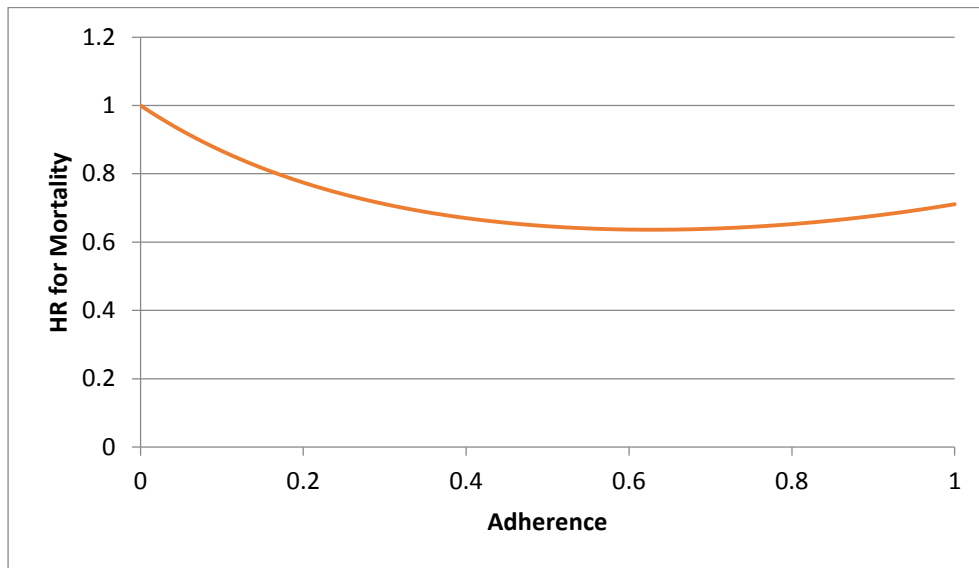
Supplementary Table 2: List of antidepressants and ATC codes and summary of users

according to drug group.

DESIPRAMINE	N06AA01
IMIPRAMINE	N06AA02
CLOMIPRAMINE	N06AA04
OPIPRAMOL	N06AA05
DIBENZEPIN	N06AA08
AMITRIPTYLINE	N06AA09
NORTRIPTYLINE	N06AA10
DOXEPIN	N06AA12
MAPROTILINE	N06AA21
FLUOXETINE	N06AB03
CITALOPRAM	N06AB04
PAROXETINE	N06AB05
SERTRALINE	N06AB06
FLUVOXAMINE	N06AB08
ESCITALOPRAM	N06AB10
PHENELZINE	N06AF03
MOCLOBEMIDE	N06AG02
MIANSERIN	N06AX03
TRAZODONE	N06AX05
MIRTAZAPINE	N06AX11
BUPROPION	N06AX12
VENLAFAXINE	N06AX16
MILNACIPRAN	N06AX17
REBOXETINE	N06AX18
DULOXETINE	N06AX21
ST. JOHN'S WORT	N06AX30

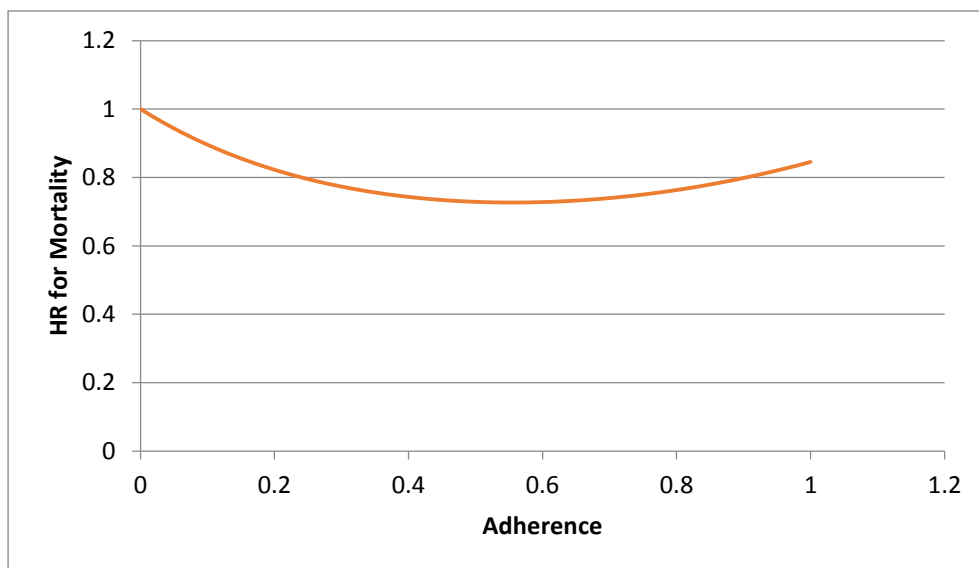| Drug group	n	%
SSRI	192697	44.9
SNRI	35951	8.4
TCA	84761	19.7
MAO	123	0.0
Others	5021	1.2

Figure 4:
a)

b)

Figure 4: Polynomial regression model of mortality hazard by continuous adherence level, adjusted for age, gender, smoking status, socioeconomic status and Charlson's comorbidity score of population with chronic Depression diagnosis: a) entire population (n=93,446). b) Sub-population (n=77,157) with more than 6 months of prescription