*Supplementary Materials:*

**Dialysis modality and mortality in elderly patients: a meta-analysis**

Seung Seok Han,* Jae Yoon Park,* Soohee Kang,† Kyoung Hoon Kim,‡ Dong-Ryeol Ryu,§ Hyunwook Kim,‖ Kwon Wook Joo,*¶ Chun Soo Lim,¶** Yon Su Kim,*¶ Dong Ki Kim*¶

*Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea; †Medical Research Collaborating Center, Seoul National University Hospital, Seoul, Korea; ‡Department of Public Health, Graduate School, Korea University, Seoul, Korea; §Department of Internal Medicine, School of Medicine, Ewha Womans University, Seoul, Korea; ‖Department of Internal Medicine, Wonkwang University College of Medicine, Sanbon Hospital, Gyeonggi-do, Korea; ¶Kidney Research Institute, Seoul National University, Seoul, Korea; **Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul, Korea

### *Statistical Analyses*

All of the analyses and calculations were performed using SPSS (SPSS version 21.0, IBM, Armonk, NY, USA) and STATA (STATA version 12.0, StataCorp LP, College Station, Texas, USA). The data are presented as means ± standard deviation for continuous variables and as proportions for categorical variables. Differences from baseline variables were analyzed using the Student's t test for continuous variables and the chi-square test for categorical variables. For the comparison of mortality between HD and PD in the Korean dataset, Cox proportional hazard model was initially applied throughout the adjustment of all the covariates; when looking at the log minus log plot, the assumption of proportional hazards was reasonable. Furthermore, other statistical approaches were used, such as the adjustment of propensity score, one-to-one matching model based on propensity score, and marginal structural model using an inverse probability of treatment weight. Propensity scores for PD prescription were calculated via a logistic regression model that included all the covariates as predictors. The goodness-of-fit for the logistic model was assessed using the Hosmer-Lemeshow test. Following that, the nearest neighbor matching was conducted to create one-to-one correspondences between patients in the HD and PD groups. Balance for comparing the distribution of baseline covariates between groups after matching was assessed by the standardized difference (38). To weight the inverse probability of treatment, the "iweight" function in Stata was used. Based on these methods, the HRs and 95% confidence intervals for mortality rates with PD (vs. HD) were calculated. A *P* value of less than 0.05 was considered significant for the estimated HRs. For the meta-analysis, random-effects models were applied due to the anticipated between-country or between-cohort heterogeneity in clinical practice. Heterogeneity across studies was summarized with the $I^2$ statistic. Some studies analyzed data according to subgroups, such as diabetes mellitus. Accordingly,

combined HRs were calculated from these subgroup results. Publication bias was identified by Egger's and Begg's tests of funnel plot asymmetry.

## *Additional Korean Results and Supplementary Figures*

### Baseline Characteristics for additional analyses

During a follow-up period, 1756 patients (13.4%) died within 90 days of dialysis and 4736 patients (36.2%) died 90 days and after. The patients who died within 90 days had more severe comorbidities than the patients who died after 90 days or the patients who survived. However, the proportion of patients with diabetes mellitus was lower in those dying within 90 days than in those who died after 90 days or those who survived (Table S1). Baseline characteristics for one-to-one matching groups or intention-to-treat analysis were shown in Table S2.

### Additional analyses of the comparison between HD and PD

A propensity score was calculated based on all the covariates ($P$ = 0.78 by Hosmer-Lemeshow test). Using the propensity score, three additional methods were applied: the adjustment of propensity score, one-to-one matching model, and marginal structural model. After matching with propensity score, there was a balance of baseline characteristics between HD and PD groups: all standardized differences between covariates were within ± 0.1. As a result, the difference in mortality between HD and PD remained significant regardless of statistical approach. When the analysis was stratified by follow-up period, the survival benefit of HD became apparent after 9 months of dialysis. This trend was similar across statistical approaches. When the study participants were limited by the intention-to-treat analysis, the results were also similar to those mentioned previously (Table S3). A sensitivity analysis using different age cut-off points showed similar results except in patients with more advanced age: no survival benefit was seen in patients aged ≥ 77 years for any dialysis

modality (Table S4).

**Stratified analyses by the diabetes mellitus**

Based on the Cox model, there was a significant interaction with diabetes mellitus for the relationship with mortality ($P < 0.05$). However, there were no important interactions between dialysis modality and age group in this elderly subset. Therefore, we conducted an analysis that was stratified by the presence of diabetes mellitus (Table S5). The PD group had a higher mortality rate than the HD group irrespective of diabetes mellitus status, which became prominent after 9 months. When the statistical significances or HRs were reviewed, the survival discrepancy between HD and PD was more prominent in the presence of diabetes mellitus than in its absence.

38. Austin PC: Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 28: 3083-3107, 2009.

**Supplementary figure legends**

Figure S1. Survival curves assessed from the multivariate Cox proportional model. Blue and red lines represent hemodialysis and peritoneal dialysis groups, respectively.

Figure S2. Funnel plot for all studies included in the meta-analysis.

Figure S3. Subgroup meta-analysis of mortality in peritoneal dialysis compared with hemodialysis grouped by diabetes mellitus (A) and dialysis start time (B) after excluding studies in which subgroup HRs were not reported. (C): Subgroup meta-analysis by dialysis start time, including only studies which had subgroup results from both the 1990s and 2000s. Subgroup meta-analysis by dialysis duration is not shown as a supplementary figure, because all studies described HRs for analysis of the dialysis duration subgroup (see Figure 5B).

Figure S4. Subgroup meta-analysis of mortality in patients aged ≥ 70 years on peritoneal dialysis compared with patients on hemodialysis.

Table S1. Baseline characteristics of study participants according to the timeframes of mortality

| | Death < 90 days (n = 1756) | Death ≥ 90 days (n = 4736) | Survived (n = 6573) |
|---|---|---|---|
| Age (years) | 74.3 ± 6.00 | 72.8 ± 5.69 ‡ | 71.2 ± 5.03 ‡ |
| Male sex (%) | 54.9 | 55.9 | 53.2 |
| Health security system | | | |
| National Health Insurance | 85.4 | 87.2 * | 90.9 ‡ |
| Medical Aid | 14.6 | 12.8 | 9.1 |
| Hospital classification | | | |
| General hospital | 97.2 | 94.6 ‡ | 92.4 ‡ |
| Hospital | 2.4 | 3.1 | 2.2 |
| Clinic | 0.4 | 2.3 | 5.4 |
| Medical comorbidities (%) | | | |
| Diabetes mellitus | 42.5 | 56.6 ‡ | 54.6 ‡ |
| Myocardial infarction | 7.7 | 7.0 | 4.7 ‡ |
| Congestive heart failure | 23.4 | 22.1 | 17.0 ‡ |
| Peripheral vascular disease | 9.1 | 8.8 | 7.9 |
| Cerebrovascular disease | 24.1 | 22.6 | 16.1 ‡ |
| Dementia | 6.0 | 4.0 ‡ | 2.5 ‡ |
| Chronic pulmonary disease | 30.9 | 23.7 ‡ | 21.2 ‡ |
| Connective tissue disease | 4.5 | 3.5 | 2.9 † |
| Peptic ulcer disease | 20.5 | 17.2 † | 17.0 † |
| Liver disease | 11.2 | 9.3 * | 8.3 ‡ |
| Hemiplegia | 3.8 | 2.4 † | 1.7 ‡ |
| Cancer | 17.9 | 10.8 ‡ | 6.5 ‡ |
| Charlson comorbidity index score | 3.0 ± 2.38 | 2.9 ± 2.03 * | 2.5 ± 1.85 ‡ |

Comparisons were evaluated using the chi-squared test for categorical variables and the Student's t-test for continuous variables between the groups with death < 90 days and ≥ 90 days, or the groups with death < 90 days and without death.

*$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$.

Table S2. Baseline characteristics for one-to-one matching or intention-to-treat analyses

| | 1 : 1 matching | | | | Intention-to-treat | | |
|---|---|---|---|---|---|---|---|
| | Total (n = 4780) | HD (n = 2390) | PD (n = 2390) | Standardized difference | Total (n = 11329) | HD (n = 9210) | PD (n = 2119) |
| Age (years) | 71.4 ± 5.14 | 71.5 ± 5.15 | 71.4 ± 5.12 | -0.011 | 71.9 ± 5.38 ‡ | 72.1 ± 5.46 | 71.1 ± 4.95 |
| Male sex (%) | 53.3 | 54.1 | 52.6 | 0.023 | 54.3 | 54.5 | 53.4 |
| Health security system | | | | 0.055 | | | |
| National Health Insurance | 90.0 | 90.8 | 89.1 | | 89.3 | 89.2 | 89.8 |
| Medical Aid | 10.0 | 9.2 | 10.9 | | 10.7 | 10.8 | 10.2 |
| Hospital classification | | | | -0.013 | | | |
| General hospital | 99.2 | 99.1 | 99.2 | | 93.3 ‡ | 91.9 | 99.3 |
| Hospital | 0.7 | 0.8 | 0.6 | | 2.6 | 3.1 | 0.6 |
| Clinic | 0.1 | 0.2 | 0.1 | | 4.1 | 5.0 | 0.1 |
| Medical comorbidities (%) | | | | | | | |
| Diabetes mellitus | 57.0 | 57.4 | 56.5 | -0.026 | 55.4 * | 54.9 | 57.6 |
| Myocardial infarction | 9.2 | 8.7 | 9.6 | 0.010 | 5.7 ‡ | 5.0 | 8.8 |
| Congestive heart failure | 24.6 | 24.8 | 24.4 | 0.003 | 19.1 ‡ | 18.2 | 22.9 |
| Peripheral vascular disease | 7.5 | 6.9 | 8.0 | 0.005 | 8.3 | 8.4 | 7.6 |
| Cerebrovascular disease | 17.2 | 17.1 | 17.4 | 0.021 | 18.8 † | 19.3 | 16.6 |
| Dementia | 2.4 | 2.1 | 2.8 | 0.028 | 3.1 | 3.2 | 2.5 |
| Chronic pulmonary disease | 20.1 | 19.0 | 21.1 | 0.018 | 22.3 * | 22.7 | 20.5 |
| Connective tissue disease | 2.9 | 2.6 | 3.2 | 0.028 | 3.2 | 3.2 | 3.1 |
| Peptic ulcer disease | 15.7 | 15.1 | 16.4 | 0.016 | 17.0 | 17.3 | 16.0 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Liver disease | 7.1 | 6.7 | 7.6 | 0.029 | 8.8 * | 9.1 | 7.5 |
| Hemiplegia | 1.4 | 1.2 | 1.6 | 0.015 | 2.0 * | 2.2 | 1.4 |
| Cancer | 4.9 | 4.8 | 4.9 | 0.025 | 8.3 ‡ | 9.2 | 4.5 |
| Charlson comorbidity index score | | | | | 2.6 ± 1.94 * | 2.7 ± 1.96 | 2.6 ± 1.85 |

Statistical differences between dialysis modalities were calculated.

*$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$.

Standardized difference was calculated after matching with propensity score; Charlson comorbidity index score was not included in the logistic model for propensity score.

HD, hemodialysis; PD, peritoneal dialysis.

Table S3. Hazard ratios of mortality in peritoneal dialysis group compared with hemodialysis group in the subjects for intention-to-treat analysis

| | Covariates adjusted | | Propensity score adjusted | | Marginal structural model | | 1 : 1 matching | |
|---|---|---|---|---|---|---|---|---|
| Period | HR (95% CI) | *P* | HR (95% CI) | *P* | HR (95% CI) | *P* | HR (95% CI) | *P* |
| < 3 months | Not calculated | – | Not calculated | – | Not calculated | – | Not calculated | – |
| 3–6 months | 1.02 (0.88–1.19) | 0.81 | 1.02 (0.87–1.19) | 0.81 | 0.99 (0.93–1.05) | 0.70 | 1.05 (0.86–1.28) | 0.62 |
| 6–9 months | 1.20 (1.00–1.45) | 0.06 | 1.20 (1.00–1.45) | 0.06 | 1.00 (0.92–1.08) | 0.92 | 1.15 (0.91–1.47) | 0.24 |
| 9–12 months | 1.32 (1.08–1.60) | 0.006 | 1.32 (1.08–1.61) | 0.006 | 1.15 (1.06–1.25) | 0.001 | 1.34 (1.03–1.73) | 0.03 |
| 1–2 years | 1.43 (1.26–1.62) | < 0.001 | 1.43 (1.26–1.62) | < 0.001 | 1.22 (1.15–1.28) | < 0.001 | 1.52 (1.28–1.81) | < 0.001 |
| 2–3 years | 1.59 (1.33–1.89) | < 0.001 | 1.57 (1.32–1.88) | < 0.001 | 1.46 (1.36–1.58) | < 0.001 | 1.53 (1.21–1.94) | < 0.001 |
| Overall | 1.30 (1.21–1.39) | < 0.001 | 1.30 (1.21–1.39) | < 0.001 | 1.13 (1.10–1.16) | < 0.001 | 1.32 (1.21–1.45) | < 0.001 |

HR, hazard ratio, CI, confidence interval.

Table S4. Hazard ratios of mortality in peritoneal dialysis group compared with hemodialysis group using the covariate-adjusted model

| Cut-off points | Subject no. | HR (95% CI) | *P* |
|---|---|---|---|
| ≥ 65 years old | 13065 | 1.20 (1.13–1.28) | < 0.001 |
| ≥ 66 years old | 12007 | 1.21 (1.14–1.29) | < 0.001 |
| ≥ 67 years old | 10993 | 1.20 (1.12–1.28) | < 0.001 |
| ≥ 68 years old | 9984 | 1.18 (1.10–1.27) | < 0.001 |
| ≥ 69 years old | 9046 | 1.19 (1.10–1.28) | < 0.001 |
| ≥ 70 years old | 8126 | 1.19 (1.10–1.28) | < 0.001 |
| ≥ 71 years old | 7127 | 1.20 (1.11–1.31) | < 0.001 |
| ≥ 72 years old | 6284 | 1.18 (1.08–1.29) | < 0.001 |
| ≥ 73 years old | 5444 | 1.16 (1.05–1.27) | 0.003 |
| ≥ 74 years old | 4669 | 1.16 (1.05–1.29) | 0.004 |
| ≥ 75 years old | 4017 | 1.15 (1.03–1.28) | 0.01 |
| ≥ 76 years old | 3427 | 1.15 (1.02–1.30) | 0.02 |
| ≥ 77 years old | 2843 | 1.13 (0.99–1.29) | 0.07 |
| ≥ 78 years old | 2320 | 1.12 (0.97–1.29) | 0.13 |
| ≥ 79 years old | 1874 | 1.13 (0.96–1.32) | 0.14 |
| ≥ 80 years old | 1476 | 1.07 (0.89–1.29) | 0.47 |

HR, hazard ratio; CI, confidence interval.

Table S5. Subgroup analysis of mortality comparison between peritoneal dialysis and hemodialysis

| | Covariates adjusted | | Propensity score adjusted | | Marginal structural model | | 1 : 1 matching | |
|---|---|---|---|---|---|---|---|---|
| Period | HR (95% CI) | *P* | HR (95% CI) | *P* | HR (95% CI) | *P* | HR (95% CI) | *P* |
| < 9 months | | | | | | | | |
| Non-DM | 0.92 (0.81–1.05) | 0.22 | 0.90 (0.79–1.03) | 0.12 | 1.69 (1.60–1.76) | < 0.001 | 0.96 (0.81–1.13) | 0.62 |
| DM | 1.09 (0.97–1.24) | 0.15 | 1.10 (0.97–1.25) | 0.12 | 1.62 (1.54–1.70) | < 0.001 | 1.12 (0.96–1.31) | 0.15 |
| ≥ 9 months | | | | | | | | |
| Non-DM | 1.44 (1.25–1.66) | < 0.001 | 1.41 (1.22–1.62) | < 0.001 | 1.38 (1.30–1.45) | < 0.001 | 1.41 (1.17–1.69) | < 0.001 |
| DM | 1.49 (1.33–1.67) | < 0.001 | 1.50 (1.34–1.68) | < 0.001 | 1.52 (1.45–1.60) | < 0.001 | 1.54 (1.34–1.78) | < 0.001 |
| Overall | | | | | | | | |
| Non-DM | 1.11 (1.01–1.23) | 0.03 | 1.09 (0.99–1.20) | 0.08 | 1.11 (1.07–1.15) | < 0.001 | 1.15 (1.01–1.30) | 0.03 |
| DM | 1.28 (1.18–1.40) | < 0.001 | 1.29 (1.19–1.40) | < 0.001 | 1.10 (1.06–1.14) | < 0.001 | 1.33 (1.20–1.48) | < 0.001 |

HR, hazard ratio, CI, confidence interval; DM, diabetes mellitus.

Figure S1.

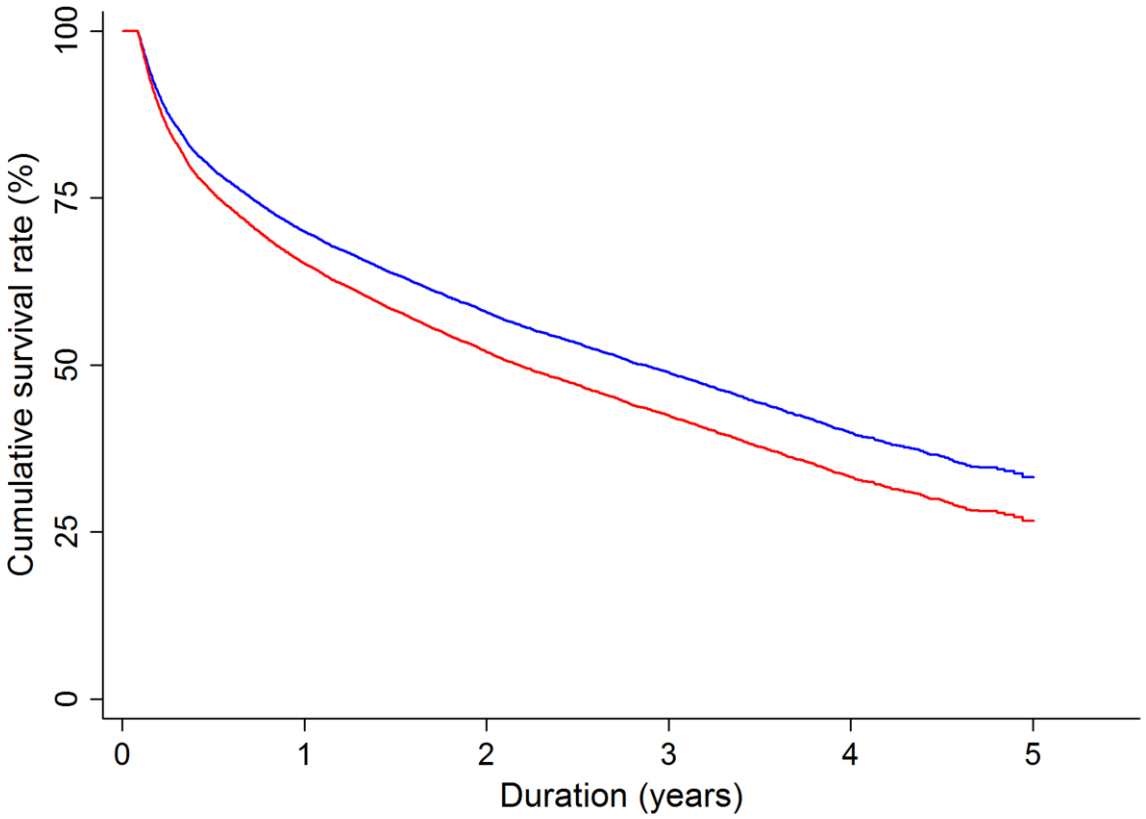

Cumulative survival rate (%)
0
25
50
75
100
0
1
2
3
4
5
Duration (years)

Figure S2.

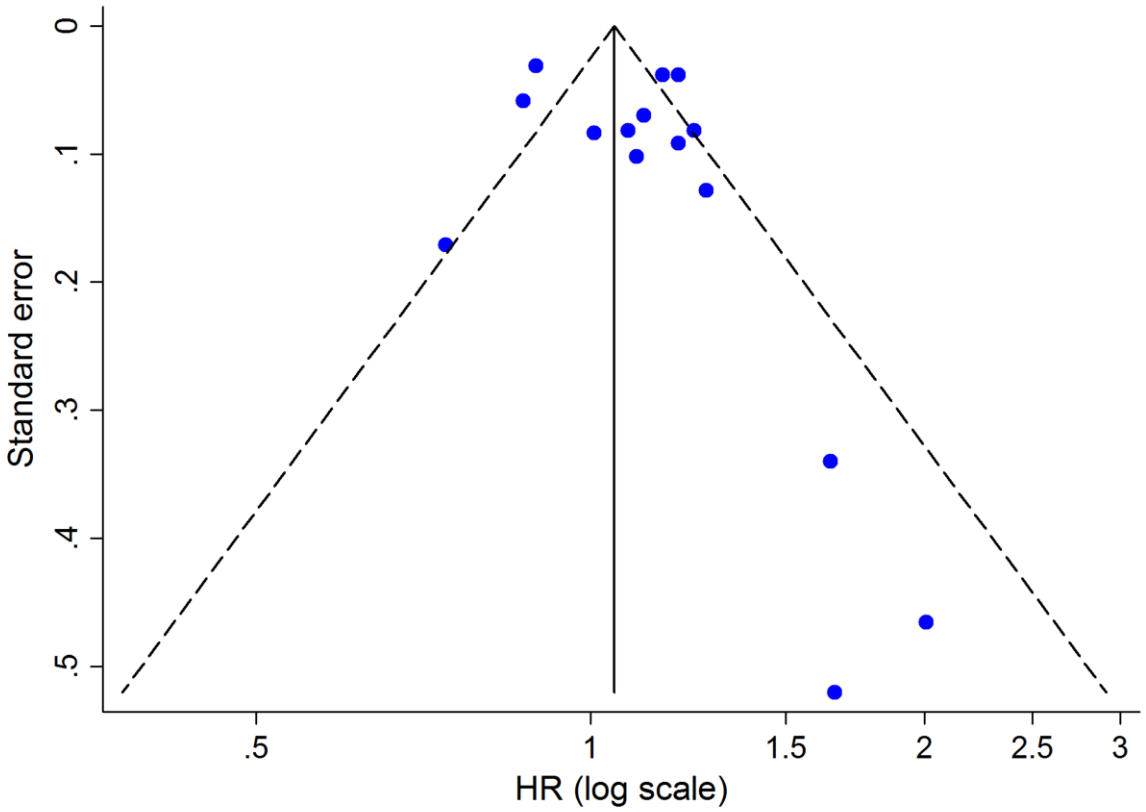


Figure S3A.

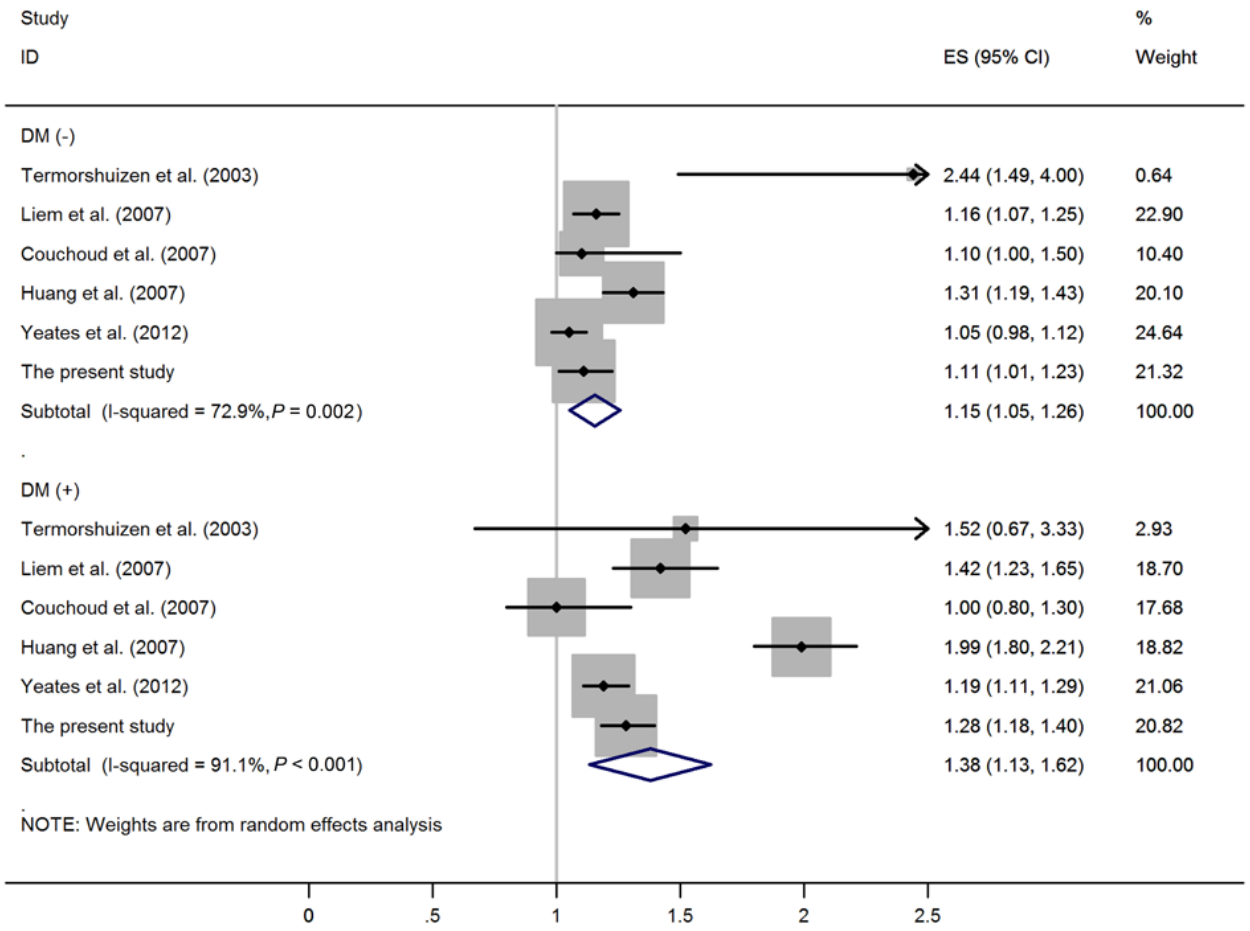

Study
ID
ES (95% CI)
%
Weight
DM (-)
Termorshuizen et al. (2003) 2.44 (1.49, 4.00) 0.64
Liem et al. (2007) 1.16 (1.07, 1.25) 22.90
Couchoud et al. (2007) 1.10 (1.00, 1.50) 10.40
Huang et al. (2007) 1.31 (1.19, 1.43) 20.10
Yeates et al. (2012) 1.05 (0.98, 1.12) 24.64
The present study 1.11 (1.01, 1.23) 21.32
Subtotal (I-squared = 72.9%, P = 0.002) 1.15 (1.05, 1.26) 100.00
DM (+)
Termorshuizen et al. (2003) 1.52 (0.67, 3.33) 2.93
Liem et al. (2007) 1.42 (1.23, 1.65) 18.70
Couchoud et al. (2007) 1.00 (0.80, 1.30) 17.68
Huang et al. (2007) 1.99 (1.80, 2.21) 18.82
Yeates et al. (2012) 1.19 (1.11, 1.29) 21.06
The present study 1.28 (1.18, 1.40) 20.82
Subtotal (I-squared = 91.1%, P < 0.001) 1.38 (1.13, 1.62) 100.00
NOTE: Weights are from random effects analysis
0
.5
1
1.5
2
2.5

Figure S3B.

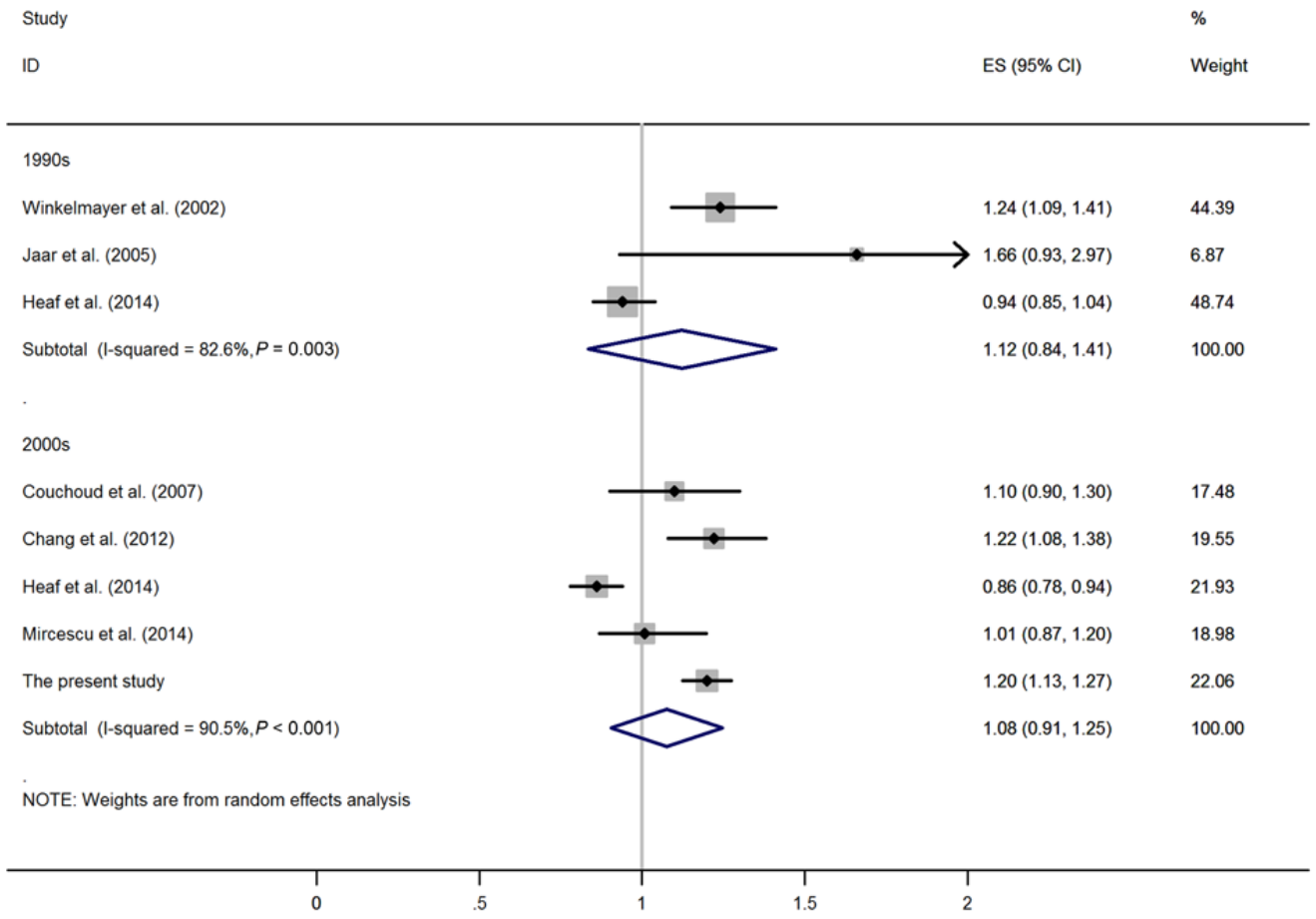

Study
ID
ES (95% CI)
%
Weight
1990s
Winkelmayer et al. (2002)
1.24 (1.09, 1.41)
44.39
Jaar et al. (2005)
1.66 (0.93, 2.97)
6.87
Heaf et al. (2014)
0.94 (0.85, 1.04)
48.74
Subtotal (I-squared = 82.6%, P = 0.003)
1.12 (0.84, 1.41)
100.00
2000s
Couchoud et al. (2007)
1.10 (0.90, 1.30)
17.48
Chang et al. (2012)
1.22 (1.08, 1.38)
19.55
Heaf et al. (2014)
0.86 (0.78, 0.94)
21.93
Mircescu et al. (2014)
1.01 (0.87, 1.20)
18.98
The present study
1.20 (1.13, 1.27)
22.06
Subtotal (I-squared = 90.5%, P < 0.001)
1.08 (0.91, 1.25)
100.00
NOTE: Weights are from random effects analysis
0
.5
1
1.5
2

Figure S3C.

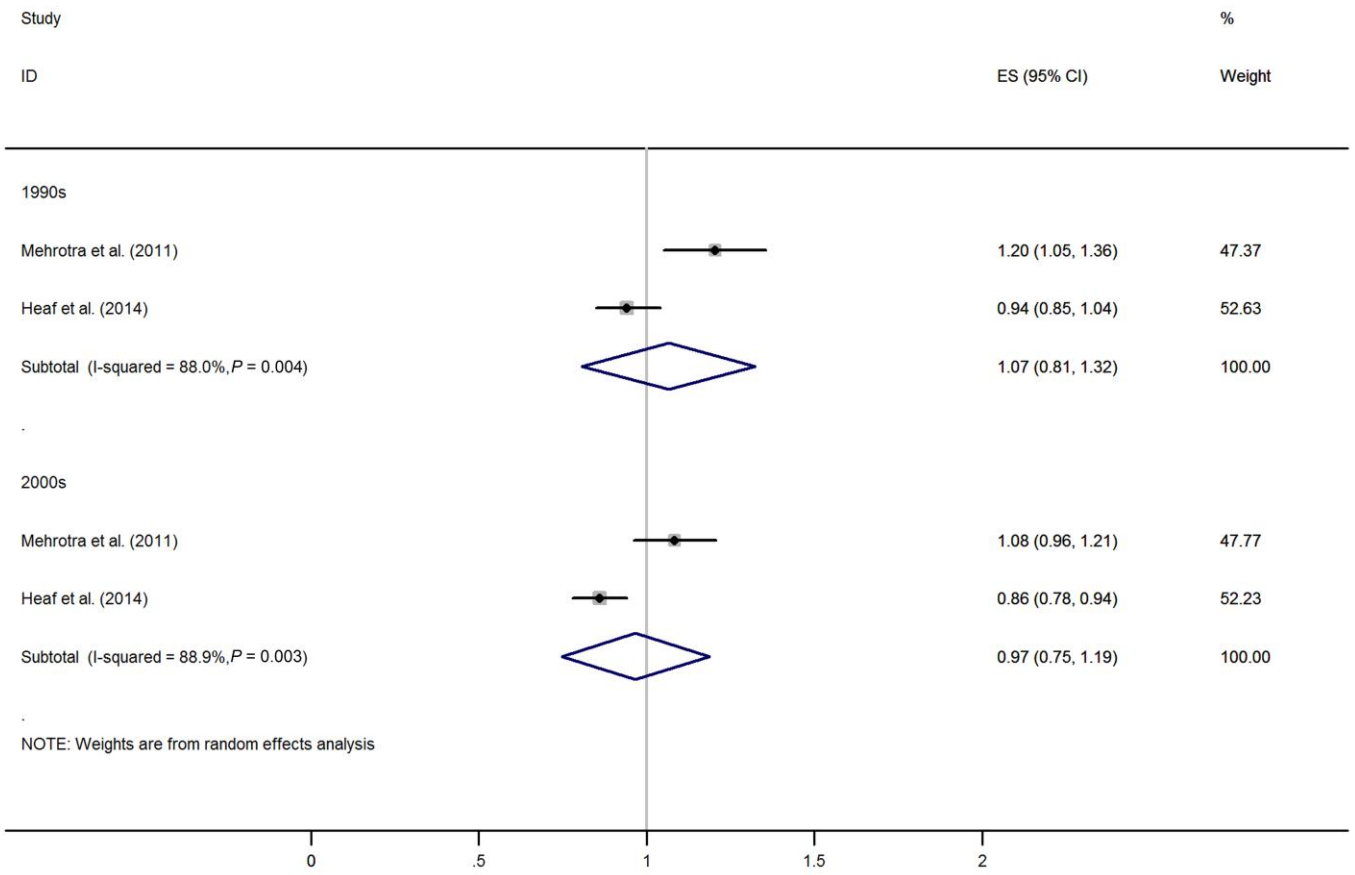
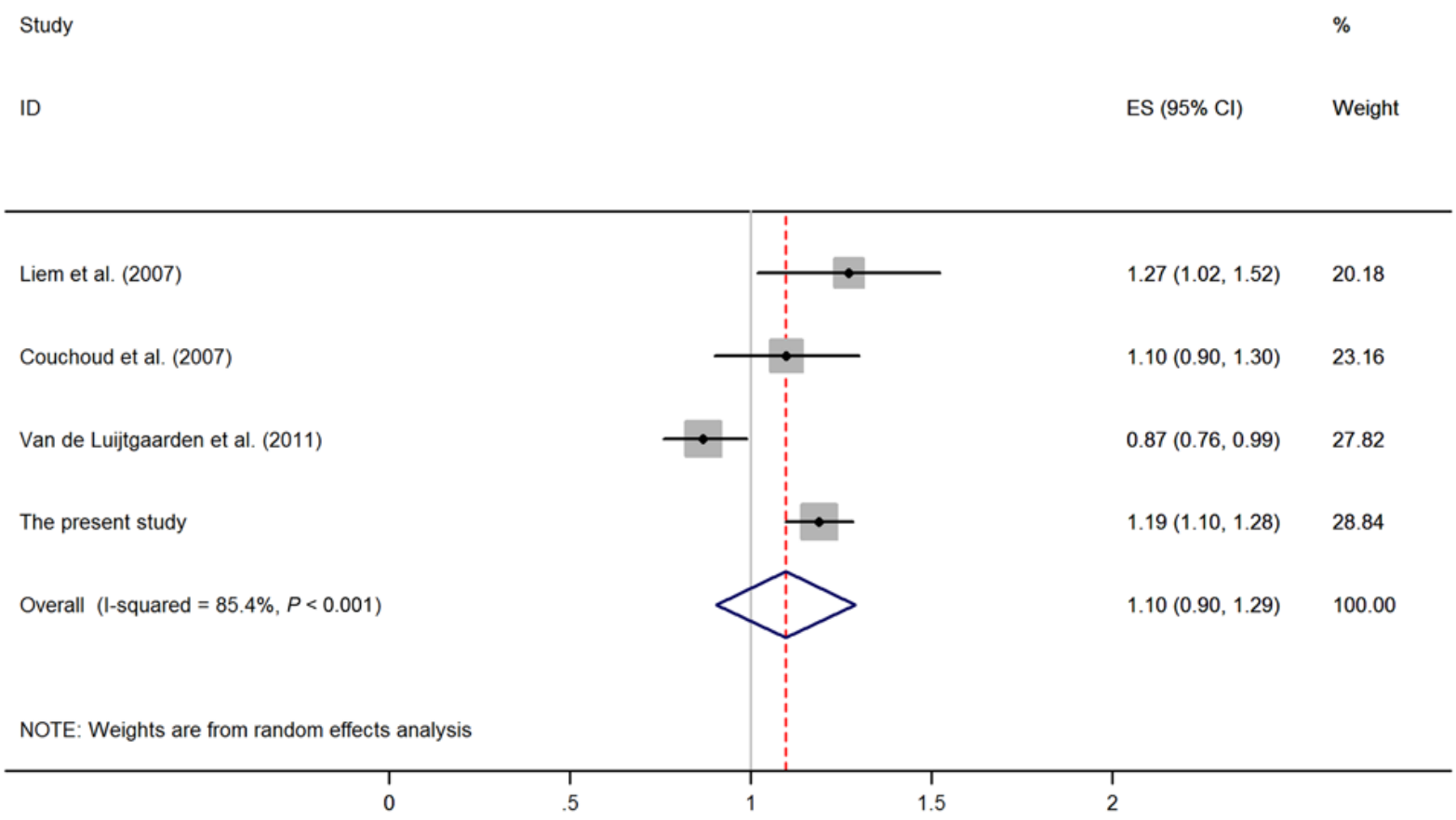

Study
ID
ES (95% CI)
%
Weight
1990s
Mehrotra et al. (2011)
1.20 (1.05, 1.36)
47.37
Heaf et al. (2014)
0.94 (0.85, 1.04)
52.63
Subtotal (I-squared = 88.0%, P = 0.004)
1.07 (0.81, 1.32)
100.00
2000s
Mehrotra et al. (2011)
1.08 (0.96, 1.21)
47.77
Heaf et al. (2014)
0.86 (0.78, 0.94)
52.23
Subtotal (I-squared = 88.9%, P = 0.003)
0.97 (0.75, 1.19)
100.00
NOTE: Weights are from random effects analysis
0
.5
1
1.5
2

Figure S4.


Study
ID
ES (95% CI)
%
Weight
Liem et al. (2007)
1.27 (1.02, 1.52)
20.18
Couchoud et al. (2007)
1.10 (0.90, 1.30)
23.16
Van de Luijtgaarden et al. (2011)
0.87 (0.76, 0.99)
27.82
The present study
1.19 (1.10, 1.28)
28.84
Overall (I-squared = 85.4%, P < 0.001)
1.10 (0.90, 1.29)
100.00
NOTE: Weights are from random effects analysis
0
.5
1
1.5
2