

Nursing Intervention on the Compliance of Hemodialysis Patients with End-Stage Renal Disease: A Meta-Analysis

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Keywords

End-stage renal disease · Nursing intervention · Dialysis compliance · Meta-analysis

Abstract

Background: Dialysis is imperative for patients with end-stage renal disease (ESRD); however, compliance ensures its efficacy. Nursing intervention has been considered to improve compliance. This meta-analysis is aimed at exploring the effects of nursing intervention on dialysis compliance.

Methods: A search was performed in the PubMed, Cochrane, and Embase databases for relevant original research articles. Studies were included or excluded based on the simultaneous consideration of quality as ranked by Jadad score and the compliance with predefined selection criteria. **Results:** A total of 817 participants were included. The results showed that nursing intervention led to significantly higher compliance with dialysis than in standard care. A pilot analysis evidenced that different intervention strategies, including educational, cognitive, and behavioral approaches, had limited effects on dialysis compliance. **Conclusion:** Nursing inter-

vention is beneficial for raising dialysis compliance, providing evidence of the need to strengthen nursing care for ESRD patients administered with dialysis in daily clinical practice.

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Introduction

In patients with chronic kidney diseases, dialysis is a critically important treatment that prolongs the survival time and improves the quality of life [1–2]. Dialysis facilitates the excretion or removal of the toxic and harmful metabolic wastes from the human body [3]. However, the poor compliance of patients might negatively influence its effects [4–6]. For example, if patients do not strictly control their daily dietary and fluid intake, more excretion power would be required, which can consequently cause bone demineralization, pulmonary edema, metabolic disorder, cardiovascular damage, and even death [2, 7].

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Nursing intervention has been progressively identified as being increasingly important to the improvement of patients' compliance with dialysis [3, 9]. Such interventions, including education, training, and behavioral introduction, which help patients gain more knowledge of dialysis and develop healthy life habits, further improve their compliance with this treatment [3, 10–13]. To date, the most commonly reported indicators for the assessment of compliance include serum phosphorus level and interdialytic weight gain (IDWG), whereas in some studies compliance has been directly evaluated and the compliance rate reported [12–14]. Recently, guidelines for compliance have been established by the World Health Organization and the National Kidney Foundation Dialysis Outcome and Quality Initiative (KDOQI) [8, 15–17].

In general, inconsistency in compliance measurements remains [12–14]. For example, some studies report biomarker changes after the intervention, which are not completely consistent with clinical outcomes [12–14]. In this meta-analysis, we searched the literature to elucidate the effects of nursing intervention on dialysis compliance and to combine compliance/noncompliance with qualitative indicators and clinic significance.

Methods

Data Sources and Searches

A computerized search was performed in the PubMed, Cochrane, and Embase databases (from 2000 to 2016, totally 190 months) for original research articles using the following keywords: (educational OR cognitive OR behavioral) AND (intervention OR nursing OR care) AND (dialysis OR hemodialysis OR renal disease OR kidney) AND (compliance OR adherence OR IDWG OR serum phosphorus). The year was preliminarily determined since the criteria for compliance had dramatically changed; the study design and quality before 2000 were poor in the large majority of cases.

The following selection criteria were applied: (i) population: end-stage kidney disease patients administered with hemodialysis or peritoneal dialysis, which was done in a hospital or nursing home; (ii) intervention: educational, cognitive, and/or behavioral oral or video intervention performed by nurses or caregivers; (iii) comparison intervention: standard care control; (iv) outcome measures: compliance, noncompliance, IDWG, and phosphorus; and (v) study design: primarily randomized clinical trial (RCT).

Data Extraction and Quality Assessment

For each study, we recorded the first author, year of publication, sample size, study designs, and outcome measurements. To assess the eligibility, the data and the trial quality information were extracted from the articles selected for inclusion in the meta-analysis independently by 2 investigators. The extracted data were imported into a standardized Excel file and checked by an independent third investigator. Any disagreements were resolved by discussion and

consensus. The outcome measurement was the rate of compliance/noncompliance, judged based on World Health Organization and KDOQI guidelines [8, 15–17]. The following exclusion criteria were used: (i) Attendance at less than the prescribed number of weekly dialysis treatments; (ii) Shortening of a single prescribed dialysis treatment by 10 min or more; (iii) IDWG <2.0 kg/day; (iv) Serum phosphorous <3.5 mg/dL; (v) IDWG higher than the baseline.

The methodological quality of each trial was evaluated using the Jadad scale [18]. The scale consists of 3 items describing randomization (0–2 points), blinding (0–2 points), and dropouts and withdrawals (0–1 points) in RCTs. A score of 1 is given for each of the points described. Another point is obtained when the method of randomization and/or blinding is given and is appropriate; when it is inappropriate, a point is deducted. Thus, the quality scale ranges from 0 to 5 points, and higher scores indicate better reporting. The studies are considered to be of low quality if the Jadad score is ≤ 2 and of high quality if the score is ≥ 3 [19]. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [20].

Data Analysis

All data were combined using RevMan 5.3.0 (<http://ims.cochrane.org/revman>). Compliance rates were extracted from the included literature. In some cases, the compliance rate was not directly reported in the literature and could not be attained after e-mailing to the authors. Thus, we derived it by computerized statistical simulation on the premise of an assumption of a normal distribution of IDWG or serum phosphorus. Then, we estimated the compliance rate by the "NORM.DIST" function using Microsoft "Excel" software according to the aforementioned criteria. For all the included studies, the extracted or derived outcome was based on the time point of primary endpoint or on variables at the last visit if no primary endpoints were reported. The outcome included the relative differences (RD) and pooled RD. Meanwhile, a random effects model was adopted [21], because in some examinations, the investigator included patients who met the noncompliance criteria and intervened. However, some authors included all CKD patients who underwent dialysis. For this reason, RD was more reliable than the OR when we assumed that the baseline in specific study was balanced. Furthermore, we conducted a sensitivity analysis of OR, and the outcome was also reported. Heterogeneity across studies was tested using the I^2 statistic, a quantitative measure of inconsistency across studies. Studies with an I^2 from 25 to 50% were considered to have low heterogeneity, I^2 from 50 to 75% indicated moderate heterogeneity, and $I^2 > 75%$ exhibited high heterogeneity [22]. If $I^2 > 50%$, the potential sources of heterogeneity were identified by sensitivity analyses conducted by omitting one study in each turn and investigating the influence of a single study on the overall pooled estimate. A subgroup analysis was performed based on different durations. The potential publication bias was assessed by visual inspection of the Begg funnel plots. $p < 0.05$ was considered significant.

Results

Search Results

The initial search yielded 88 relevant publications, of which 64 were excluded on the basis of their titles and

Table 1. Characteristics of randomized controlled trials included in the meta-analysis

Author, year	Means of age, years (I/C)	Male/female	Sample size (I/C)	Withdrawal number (I/C)	Intervention (experimental group)	Measurements of outcome	Study design/Jadad score
Wu et al. [27], 2015	NA	56/44	50/50	NA	Educational, psychological, dietary intervention	Compliance	RCT, open/3
Zhang et al. [25], 2016	45.6/45.3	107/113	110/110	NA	Emotional, cognitive, behavioral intervention	Compliance	RCT, open/3
Braden et al. [10], 2005	65.2/63.6	38/32	35/35	12/7	Educational intervention	Compliance	RCT, open/4
Jennifer et al. [13], 2009	60.0/60.1	14/1	8/7	NA	Cognitive, behavioral intervention	Weight	RCT, open/3
Cui et al. [26], 2009	48.6/49.0	46/33	39/40	NA	Cognitive, behavioral intervention	Compliance	RCT, open/3
Howren et al. [14], 2016	55.9/58.2	78/41	61/58	NA	Behavioral intervention	IWDG	RCT, open/3
Tsay et al. [24], 2003	57.5/57.9	28/36	32/32	1/1	Educational training	IWDG	RCT, open/3
Ford et al. [23], 2004	NA	24/39	35/35	4/3	Diet education	Phosphorus	RCT, open/3
Sharp et al. [12], 2005	56.1/52.5	38/18	29/27	NA	Cognitive behavior therapy	IWDG	RCT, open/4

I/C, intervention group/control group; NA, not applicable; RCT, randomized clinical trial.

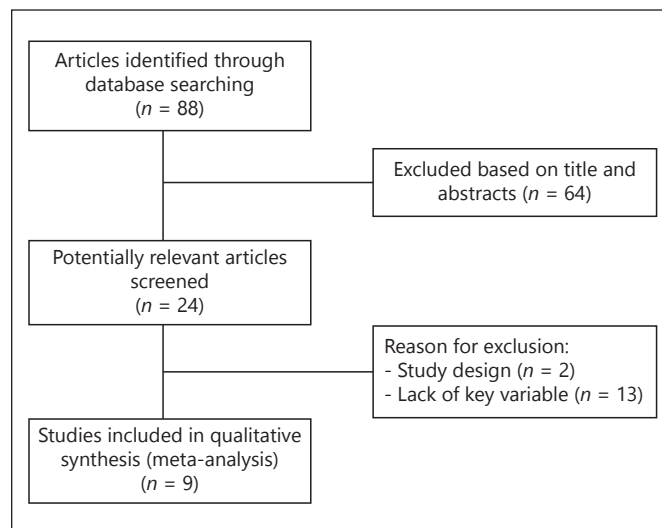


Fig. 1. Flow chart of the search strategy for the meta-analysis.

abstracts, because they were duplicate studies, reviews, non-randomized studies, or irrelevant to our analysis (Fig. 1). Twenty-four potentially relevant studies were identified for full-text analysis, but 2 were excluded for low quality, 13 were excluded because of a lack of key data for analysis. Finally, 9 RCT studies were selected, 6 published in English [10, 12–14, 23–24] and 3 in Chinese [25–27].

Study Characteristics

The main characteristics of the 9 studies published between 2003 and 2016 are listed in Table 1. The sample size of the trials ranged from 15 to 220 (a total of 817 patients, 429 males and 388 females). The patients were mainly from China, the USA, and the UK, and thus represented Asia, Europe, and Northern America to eliminate regional confounding. Although the intervention methods utilized in the experimental group were inconsistent, all interventions were provided by professional nurses. The Jadad score ranged from 3 to 4.

Meta-analysis of Outcome Measures

The aggregated results of the studies showed that nursing intervention was associated with significantly increased compliance to dialysis (RD 0.15, 95% CI 0.07–0.23, $p = 0.0003$, for heterogeneity, $I^2 = 44%$, $p = 0.07$; OR 2.17, 95% CI 1.38–3.42, $p = 0.0008$, for heterogeneity, $I^2 = 45%$, $p = 0.07$; Fig. 2). The results of RD suggested that the patients with nursing intervention had 15% higher dialysis compliance compared to the patients given standard

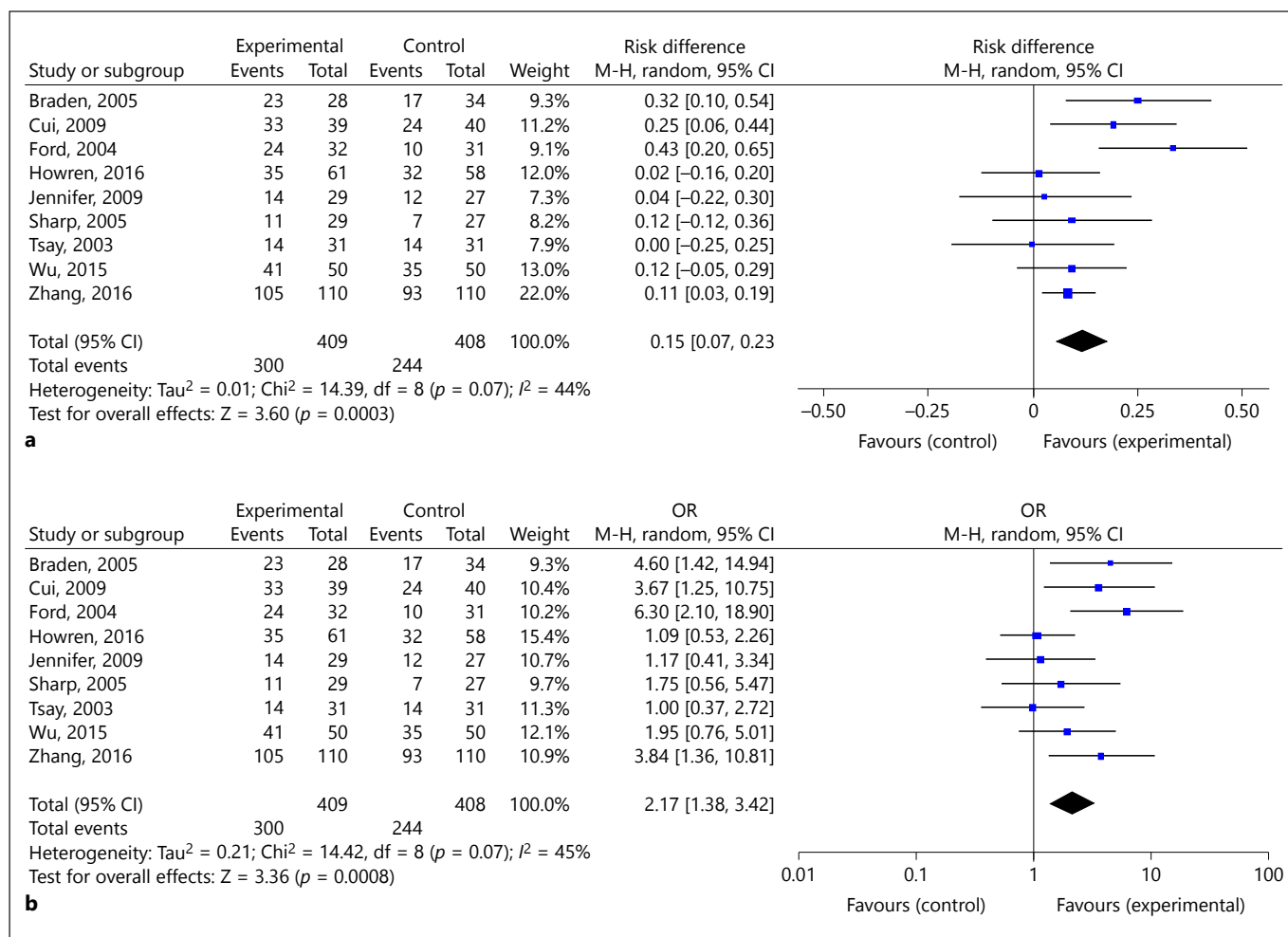


Fig. 2. a, b A forest plot of the meta-analyses of RCTs comparing the compliance with dialysis in the nursing intervention group and the control group. Each block represents a study and the area of each block is proportional to the precision of the mean treatment

effect in that study. The horizontal line represents each study's 95% CI for the treatment effect. The center of the diamond is the average treatment effect across studies, and the width of the diamond denotes its 95% CI.

care only. For sensitivity analysis, the results of OR also indicated that patients given additional nursing intervention had over 2-fold more possibilities to comply with dialysis compared to those with the standard care, which supported the results obtained for RD. In addition, we performed a funnel plot to establish the publication bias. However, the limitation of the number of RCTs made the interpretations of the results complicated (Fig. 3).

The aggregated RD of 5 studies carried out in Europe and America was 0.19 (95% CI 0.02–0.35), $p = 0.03$, which was 4% higher than the average effect of 15%. In contrast, the aggregated RD of 4 studies conducted in Asia, mainly in mainland China, was 0.12 (95% CI 0.06–0.18), $p = 0.0003$, was 3% lower than the average effect. Taken to-

gether, it seemed that the effect of the intervention was more significant in Western countries than in China (Fig. 4a). Furthermore, the effect of different intervention methods was compared (Fig. 4b). The aggregated RD of 5 studies involving behavioral intervention was 0.11 (95% CI 0.05–0.17), $p = 0.0006$; the aggregated RD of 4 studies with cognitive intervention was 0.12 (95% CI 0.06–0.19), $p = 0.0003$; the aggregated RD of 3 studies that used educational intervention was 0.15 (95% CI –0.02 to 0.32), $p = 0.08$. However, from the pilot results, we could not observe significant consistencies among the 3 most commonly implemented methods, while the figures were not different dramatically.

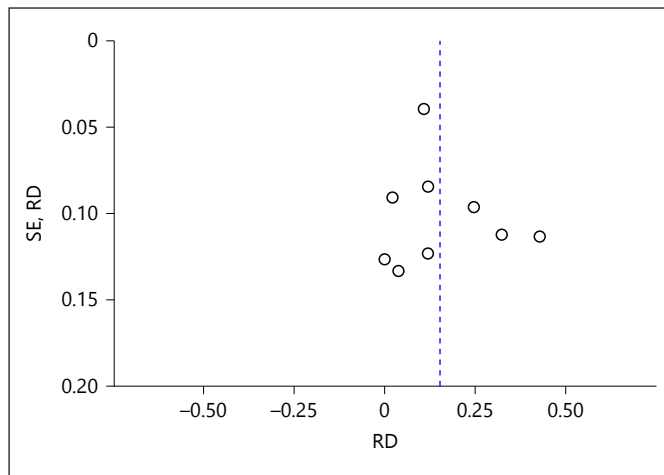


Fig. 3. A funnel plot of the compliance (RD).

Discussion

Compliance to a specific therapeutic regimen is critical for obtaining optimal effects, but its importance has always been underestimated [3, 28–29]. The significance of dialysis therapy needs to be highlighted since the patients undergoing this intervention have to not only adhere to the treatment regimen requirements, but also change their lifestyle, optimize their diet, and so on. [28–31]. Thus, nursing intervention, which is usually readily available and affordable, is important for the improvement of compliance. This meta-analysis showed that nursing intervention facilitated patient's compliance to dialysis, and the mean effect was 15% in total, which means that nursing intervention lead to an increase of 15% in the compliance of patients compared to that in standard care. Thus, the more extensive dissemination and earnest utilization of the practice of such an intervention can prolong the survival of ESRD patients [32].

Nursing intervention, including the application of educational, cognitive, behavioral, and dietary methods, has been shown to exert favorable effects on the physical and emotional health of ESRD patients [10, 12–14]. Nevertheless, the results reported in the literature are inconsistent; the measurements of the effects vary and lack comparability. For instance, weight and IDWG were used as main endpoints in some trials [12–14, 24], whereas in others, biomarkers, such as phosphorus, Kt/V, or albumin were employed [23, 33]. In the present study, we combined different indicators and transferred them to a more clinically meaningful and comparable indicator, which was in compliance to dialysis. Further, in this meta-analysis, we

preliminarily explored the effect of different intervention methods and found no significant difference between them, but potential bias from cultural and ethical gap, and the subtle difference in the same category of intervention from different studies hampered the possibility of drawing a conclusion.

The national difference was more significant, and the effect of the intervention in China was lower than that in Europe or the USA (12 vs. 19%), the effect from the western world were higher than the average effect (19 vs. 15%), while in China it was the opposite (12 vs. 15%), indicating first that Chinese patients may be reluctant to follow nursing intervention and lack essential health consciousness [34–36], and second that Chinese nurses and caregivers need to improve their nursing strategies [37–38]. It is undeniable that patients in developed countries have access to more health resources and benefits than patients in developing countries. Herein, we can also see that the expertise and professional skills of medical staff, the acceptance and support to medical introduction of patients in China also lag [39–41]. Indeed, improving people's consciousness and willingness can be extremely difficult. Nevertheless, the Chinese government and medical sectors need to invest more effort to strengthen the infrastructure of instruction to correct the prejudice to medical staff care and attitudes [42–44].

This meta-analysis has some limitations. First, the computational transformation of biomarkers into compliance can lead to information bias and the lack of blinding in these studies because the nature of the interventions can also lead to bias. Second, the evaluation of the effect was not convenient due to the varying numbers (single, double, or multiple) of interventions used in different studies and the cultural and regional differences. Third, the relevant studies were limited both in number and quality and comparatively few could be included. Even in the included 9 studies, one seemed to have low-balanced baseline although the researcher used randomization [24]. The main strength of the present meta-analysis is the use of a unique outcome, compliance to dialysis, which was an exceedingly meaningful clinical indicator, to test the effect of nursing intervention. Moreover, aggregated RD of 15% was found that was statistically significant. Therefore, this meta-analysis also provides evidence and the basis to strengthen nursing care for ESRD patients administered with dialysis in daily clinical practice. Finally, the results suggest that for developing countries such as China, used herein as a typical example, it is critical to raise people's health consciousness and the

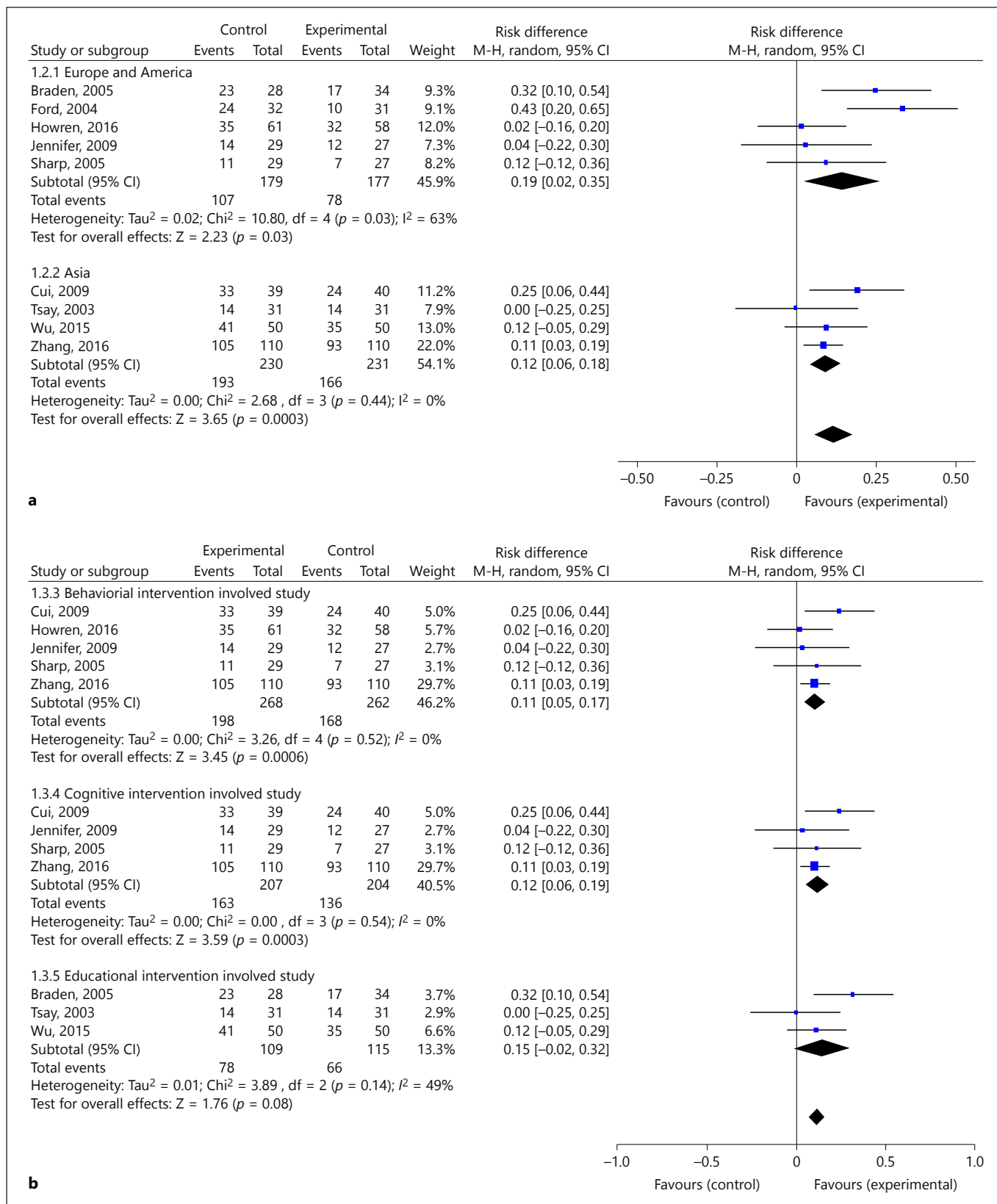


Fig. 4. a, b A forest plot of the additional analyses of RCTs comparing the compliance in the experimental and control groups.

skills of medical personnel. Taking into consideration the massive population of China, this can be of considerable importance for the well-being of global humanity [39–41, 45–46].

Conclusion

This meta-analysis showed that nursing intervention is beneficial for raising dialysis compliance, providing evidence to strengthen nursing care for ESRD patients administered with dialysis in daily clinical practice. This re-

search could inspire further studies on the topic in the future, which was a meaningful work needed to be finished.

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Disclosure Statements

All the authors declare that they have no conflict of interest.

References

- 1 Foundation NK: National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification, 2008.
- 2 USRD: USRDs 2007 annual data report. *Am J Kidney Dis* 2008;45:8–280.
- 3 Combe C, Deforges-Lasseur C, Caix J, Pommerau A, Marot D, Aparicio M: Compliance and effects of nutritional treatment on progression and metabolic disorders of chronic renal failure. *Nephrol Dial Transplant* 1993;8:412–418.
- 4 Ai-Li MA, Shao WH, Tan YS: The effect of systematic health education on the treatment compliance for patients with maintenance hemodialysis. *Chin J Dial Artif Organs* 2011;2:34–36.
- 5 Whelan P: Atlas of diseases of the kidney. *BJU Int* 2015;86:1097–1098.
- 6 Matteson ML, Russell C: Interventions to improve hemodialysis adherence: a systematic review of randomized-controlled trials. *Hemodial Int* 2010;14:370–382.
- 7 Bame SL, Petersen N, Wray NP: Variation in hemodialysis patient compliance according to demographic characteristics. *Soc Sci Med* 1993;37:1035–1043.
- 8 Saran R, Bragg-Gresham JL, Rayner HC, Goodkin DA, Keen ML, Van Dijk PC, Kurokawa K, Piera L, Saito A, Fukuhara S, et al: Nonadherence in hemodialysis: associations with mortality, hospitalization, and practice patterns in the DOPPS. *Kidney Int* 2003;64:254–262.
- 9 Leggat JE Jr, Orzol SM, Hulbert-Shearon TE, Golper TA, Jones CA, Held PJ, Port FK: Non-compliance in hemodialysis: predictors and survival analysis. *Am J Kidney Dis* 1998;32:139–145.
- 10 Manns BJ, Taub K, Vanderstraeten C, Jones H, Mills C, Visser M, McLaughlin K: The impact of education on chronic kidney disease patients' plans to initiate dialysis with self-care dialysis: a randomized trial. *Kidney Int* 2005;68:1777–1783.
- 11 Hemmati Maslakpak M, Shams S: A comparison of face to face and video-based self care education on quality of life of hemodialysis patients. *Int J Community Based Nurs Midwifery* 2015;3:234–243.
- 12 Sharp J, Wild MR, Gumley AI, Deighan CJ: A cognitive behavioral group approach to enhance adherence to hemodialysis fluid restrictions: a randomized controlled trial. *Am J Kidney Dis* 2005;45:1046–1057.
- 13 Hare J, Clark-Carter D, Forshaw M: A randomized controlled trial to evaluate the effectiveness of a cognitive behavioural group approach to improve patient adherence to peritoneal dialysis fluid restrictions: a Pilot study. *Nephrol Dial Transplant* 2014;29:555–564.
- 14 Howren MB, Kellerman QD, Hillis SL, Cvenegros J, Lawton W, Christensen AJ: Effect of a behavioral self-regulation intervention on patient adherence to fluid-intake restrictions in hemodialysis: a randomized controlled trial. *Ann Behav Med* 2016;50:167–176.
- 15 World Health Organization: Adherence to Long-Term Therapies. Evidence for Action. Geneva, World Health Organization, 2003.
- 16 Pierratos A, McFarlane P, Chan CT, Kwok S, Nesrallah G: Daily hemodialysis 2006. State of the art. *Minerva Urol Nefrol* 2006;58:99–115.
- 17 Depner TA, Daugirdas JT: Clinical Practice Guidelines and Clinical Practice Recommendations 2006 Updates Hemodialysis Adequacy Peritoneal Dialysis Adequacy Vascular Access, 2006.
- 18 Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ: Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996;17:1–12.
- 19 Gluud LL, Thorlund K, Gluud C, Woods L, Harris R, Sterne JA: Correction: reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. *Ann Intern Med* 2001;135:982–989.
- 20 Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700.
- 21 Dersimonian R, Laird N: Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177–188.
- 22 Higgins JP, Thompson SG, Deeks JJ, Altman DG: Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–560.
- 23 Ford JC, Pope JF, Hunt AE, Gerald B: The effect of diet education on the laboratory values and knowledge of hemodialysis patients with hyperphosphatemia. *J Ren Nutr* 2004;14:36–44.
- 24 Tsay SL: Self-efficacy training for patients with end-stage renal disease. *J Adv Nurs* 2003;43:370–375.
- 25 Butt AN, Choi JN: The effects of cognitive appraisal and emotion on social motive and negotiation behavior: the critical role of agency of negotiator emotion. *Hum Perform* 2006;19:305–325.
- 26 Li J: Effect of cognitive, emotional and behavioral nursing intervention on hemodialysis patients. *China Contin Med Edu* 2016;34:235–237.
- 27 Zhang Q, Yao XH, Wang HQ: Exploration of influence of nursing intervention on unhealthy mood and sleep quality of ICU conscious patients. *China Pract Med* 2017;8:169–171.
- 28 Loghman-Adham M: Medication non-compliance in patients with chronic disease: issues in dialysis and renal transplantation. *Am J Manag Care* 2003;9:155–171.
- 29 Wolcott DL, Maida CA, Diamond R, Nissen AR: Treatment compliance in end-stage renal disease patients on dialysis. *Am J Nephrol* 1986;6:329–338.
- 30 Carney EF: Peritoneal dialysis: cognitive behavioural therapy might improve patient adherence to fluid restrictions. *Nat Rev Nephrol* 2014;10:66.
- 31 Cheng YY, Wong YF, Chu BY, Lam WO, Ho YW: Rehabilitating a dialysis patient. *Perit Dial Int* 2003;23(suppl 2):S81–S83.

- 32 Devins GM, Mendelssohn DC, Barré PE, Taub K, Binik YM: Predialysis psychoeducational intervention extends survival in CKD: a 20-year follow-up. *Am J Kidney Dis* 2005; 46:1088–1098.
- 33 Sehgal AR, Leon JB, Siminoff LA, Singer ME, Bunosky LM, Cebul RD: Improving the quality of hemodialysis treatment: a community-based randomized controlled trial to overcome patient-specific barriers. *JAMA* 2002; 287:1961–1967.
- 34 Zhang R, Yin M, Xiu-Mei WU, Meng F, Liang LI: The comparative research and thought between postgraduate students and regular course students on their health consciousness, physical quality and practice. *J Nanjing Ins Phy Edu* 2005;19:84–87.
- 35 Zhang X, Ren R: Public health and people's healthy consciousness. *Med Philos* 2005;26: 1–3.
- 36 Wang L, Jun XU: Enhancement of rural inhabitants' health care consciousness of self protection by health education. *China Trop Med* 2003;16:907–913.
- 37 Tan XL: Rural nursing human resources and nursing education of china. *Educ Teach Res* 2010;1:114–116.
- 38 Duan X, Shi Y: Current status of quality evaluation of nursing care through director review and reflection from the nursing quality control centers. *Int J Clin Exp Med* 2014;7: 3737–3745.
- 39 Xu Z, Guo DJ, Yong A, Gu J, Xu X: Research and improvement of improper words and deeds of medical staff in oncology department. *Chin Med Mod Distance Educ China* 2014;12:133–134.
- 40 Zhu XY, Li-Jun QI, LWei-Bo: Improving medical staff ability of emotional management, to establish harmonious doctor-patient relationship. *Hosp Adm J Chin Peoples Liberation Army* 2008;12:1147–1148.
- 41 Zhang W, Hua L, Shao X, Wang X, Wang L: Practice and experience of cultivation and practice of medical staff core values. *China Med Herald* 2016;2:178–181.
- 42 Chan C: Increasing doctor-patient tension in china: institution and interaction. *J Beijing For Univ* 2014;33:119–123.
- 43 Cong Y: Doctor-family-patient relationship: the Chinese paradigm of informed consent. *J Med Philos* 2004;29:149–178.
- 44 Hou X, Xiao L: An analysis of the changing doctor-patient relationship in China. *J Int Bioethique* 2012;23:83–94, 177–178.
- 45 Zhang L, Wang H: Chronic kidney disease epidemic: cost and health care implications in China. *Semin Nephrol* 2009;29:483–486.
- 46 Blumenthal D, Hsiao W: Privatization and its discontents – the evolving Chinese health care system. *N Engl J Med* 2005;353:1165–1170.