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Corrigendum: Probiotics, prebiotics, and synbiotics improve uremic, inflammatory, and gastrointestinal symptoms in end-stage renal disease with dialysis: A network meta-analysis of randomized controlled trials

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A corrigendum on

[Probiotics, prebiotics, and synbiotics improve uremic, inflammatory, and gastrointestinal symptoms in end-stage renal disease with dialysis: A network meta-analysis of randomized controlled trials](#)

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In the published article, there was an error in [Figure 6](#) as published. The panel C (indole-3-acetic acid, IAA) and panel D (malondialdehyde, MDA) in [Figure 6](#) is the same as the panel C (tumor necrosis factor- α , TNF- α) and panel D (endotoxin) in [Figure 4](#). The corrected [Figure 6](#) and its caption appear below.

In the published article, there was an error in [Table 1](#) as published. The number of males in Liu et al. is wrong, 28 should be changed to 23. The corrected [Table 1](#) and its caption appear below.

In the published article, there was an error in Supplementary Figure 6. Panel A (BUN) is the same as panel B (Creatinine). The correct material statement appears below.

Supplementary Figure 6 Results of direct comparisons for other clinical outcomes. Forest plot of the effect of prebiotic, probiotic, and synbiotic supplementation on (A) BUN (mg/dl); (B) Creatinine (mg/dl); (C) Urea (mg/dl); (D) Uric acid (mg/dl).

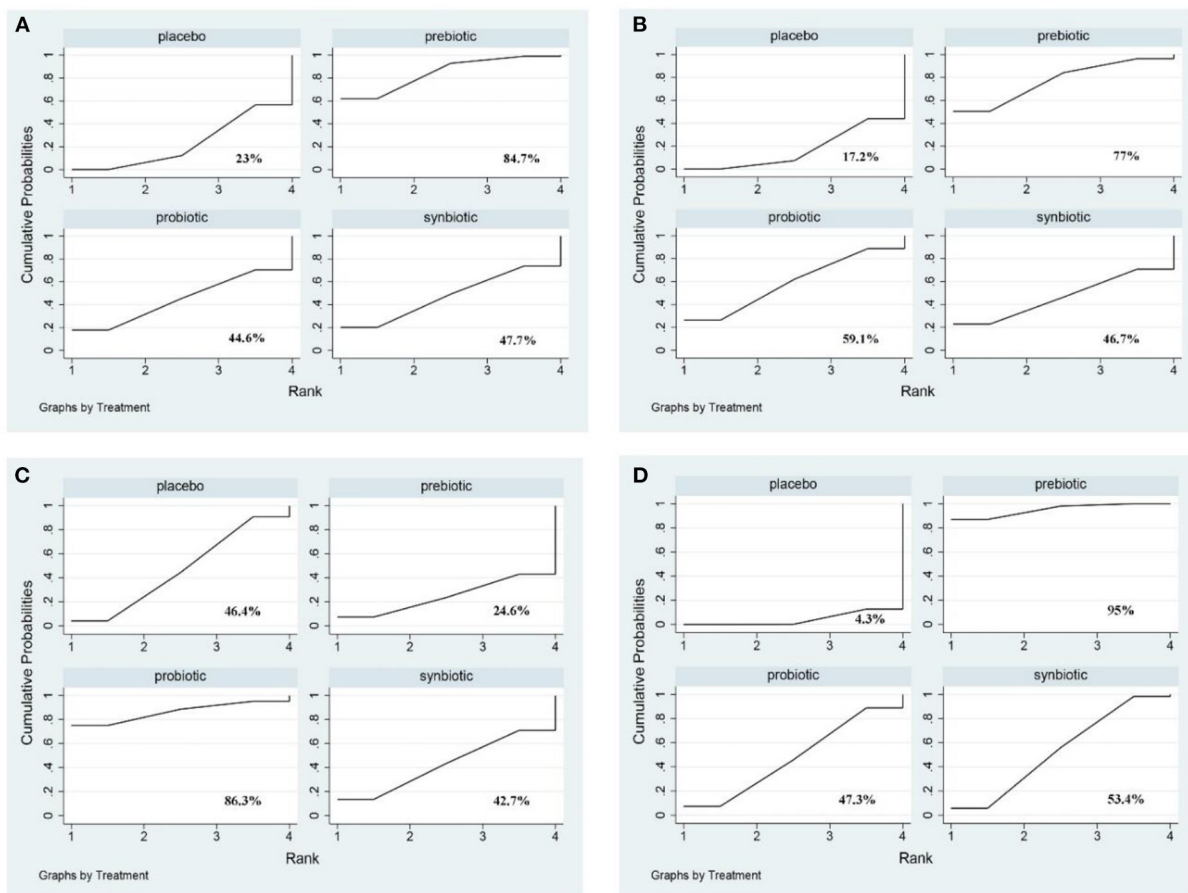


FIGURE 6

The cumulative ranking area of uremic toxins; Treatment strategies were ranked based on their probability of reducing (A) indoxyl sulfate (IS); (B) p-cresyl sulfate (PCS); (C) indole-3-acetic acid (IAA); (D) malondialdehyde (MDA) by cumulative ranking area (SUCRA). The greater the probability, the better the effect.

In the published article, there was an error in Supplementary Figure 15. The figure legend of (E) p-cresyl sulfate (PCS) should be replaced with (E) Malondialdehyde (MDA), and the original material statement was Supplementary Figure 15. Sensitivity analysis. Sensitivity analysis for the network of (A) C-reactive protein (CRP); (B) Interleukin-6(IL-6); (C) tumor necrosis factor- α (TNF- α); (D) Indoxyl sulfate (IS); (E) p-cresyl sulfate (PCS); (F) Urea. The correct material statement appears below.

Supplementary Figure 15 Sensitivity analysis. Sensitivity analysis for the network of (A) C-reactive protein (CRP); (B) Interleukin-6(IL-6); (C) tumor necrosis factor- α (TNF- α); (D) Indoxyl sulfate (IS); (E) Malondialdehyde (MDA); (F) Urea.

In the published article, there was an error. “IAA” should be changed to “MDA,” “96.8%” should be changed to “95%,” “Synbiotics” should be changed to “Probiotics,” “MDA” should be changed to “IAA,” “95.6%” should be changed to “86.3%” in the Results. A correction has been made to **Results**,

Network Meta-Analysis, Uremic Toxins. The corrected sentence appears below:

“Uremic toxins including IS, PCS, IAA, and MDA were evaluated. The outcome revealed prebiotics were superior in declining IS (prebiotics: SMD -0.43 ; 95% CI $[-0.81, -0.05]$), prebiotics and synbiotics were effective supplements on the alteration of MDA level (prebiotics: SMD -1.88 ; 95% CI $[-3.02, -0.75]$; synbiotics: SMD -0.85 ; 95% CI $[-1.67, -0.02]$) but no supplements significantly declined serum PCS, and IAA (Figure 5 and Supplementary Figure 11). With regard to IS, PCS, and MDA, prebiotics were ranked as the first therapeutic option, where the SUCRA were 84.7, 77, and 95%, respectively. Probiotics had the highest possibility in serum IAA level (SUCRA = 86.3%) (Figure 6).”

In the published article, there was an error. “Synbiotics” should be changed to “prebiotics” in the Discussion section, and “respectively” needed to be removed from another sentence. A correction has been made

TABLE 1 Characteristics of included Interventions in dialysis patients.

| Study | Country | Sample | | RCT design (blinding) | Patient | Intervention | During | Sex | | Age |
|-------------------------|----------|--------|----|--|---------|---|--------|-----|----|---------------------------------------|
| | | I | C | | | | | M | F | |
| Esgalhadó et al. (30) | Brazil | 15 | 16 | Randomized, double-blind, placebo-controlled trial | HD | I1: Prebiotic cookies (Resistant starch, Hi-Maize [®] 260, Ingredion, USA), 16 g/d C1: Placebo cookies (manioc flour, Yoki), 16 g/d | 4 w | 18 | 13 | I1:56.0 ± 7.5 C1:53.5 ± 11.5 |
| Laffin et al. (34) | Canada | 9 | 11 | Randomized, double-blind, placebo-controlled parallel trial | HD | I1: Prebiotic biscuits (HAM-RS2 Ingredion ANZ Pty Ltd Lane Cove, NSW, Australia), 20 g/d C1: Regular wheat flour, 20 g/d | 8 w | 13 | 7 | I1:53.8 ± 11.8 C1:57.6 ± 9 |
| Meksawan et al. (26) | Thailand | 9 | 9 | Randomized, double-blind, placebo-controlled crossover trial | PD | I1: Prebiotic (fructo-oligosaccharides), 20 g/d C1: Sucrose, 20 g/d | 4 w | 5 | 4 | I1:71.2 ± 6.5 C1:NA |
| Sirich et al. (22) | America | 20 | 20 | Randomized, single-blinded trial | HD | I1: Prebiotic corn (high-amylose corn starch, Hi-maize 260), 15 g/d C1: Waxy corn starch (AMIOCA), 15 g/d | 6 w | 24 | 16 | I1:54 ± 14 C1:58 ± 13 |
| Xie et al. (25) | China | 39 | 44 | Randomized controlled trial | HD | I1: Prebiotic fiber, 20 g/d C1: Placebo starch, 20 g/d | 6 w | 44 | 38 | I1:51.7 ± 15.7 C1:53.1 ± 13.2 |
| De Andrade et al. (40) | Brazil | 26 | 26 | Randomized, double-blind, placebo-controlled crossover trial | PD | I1: Prebiotic flour (Unripe Banana Flour), 21 g/d C1: Placebo sachets (6 g waxy corn starch), 21 g/d | 12 w | 14 | 12 | I1:55 ± 12 C1:NA |
| Biruete et al. (39) | Iran | 12 | 12 | Randomized, double-blind, placebo-controlled, crossover trial | HD | I1: Prebiotic (inulin: females: 10 g/day; males: 15 g/day) C1: Maltodextrin (females: 6 g/day; males: 9 g/day) | 12 w | 6 | 6 | I1:55 ± 10 C1:NA |
| Li et al. (36) | China | 15 | 15 | Randomized, double-blind, placebo-controlled, crossover trial | PD | I1: Prebiotic (inulin-type fructans), 10 g/d C1: Placebo, 10 g/d | 12 w | 6 | 9 | I1:28.84 ± 38.14 C1:NA |
| Khosroshahi et al. (32) | Iran | 23 | 21 | Randomized double-blind controlled clinical trial | HD | I1: Prebiotic crackers (20 g or 25 g of 60% resistant starch) C1: Placebo crackers (20 g or 25 g of waxy corn starch) | 32 w | 29 | 21 | I1:53.17 ± 10.15 C1:57.9 ± 13.34 |
| Lim et al. (41) | China | 25 | 25 | Randomized double-blind placebo-controlled clinical trial | HD | I1: Probiotic sachets (Lactococcus lactis subsp. Lactis LL358, Lactobacillus salivarius LS159, and Lactobacillus pentosus LPE588 at high dose, 100 billion; 13 × 10 ¹¹ cfu/day), 6 g/d C1: Placebo sachets, 6 g/d | 24 w | 20 | 30 | I1: 61.50 ± 10.30 C1:56.28 ± 12.36 |
| Shariaty et al. (16) | Iran | 18 | 18 | Randomized, double-blind, parallel group, placebo-controlled trial | HD | I1: Probiotic capsule (Lactobacillus acidophilus, Bifidobacterium and Streptococcus thermophilus (beneficial bacteria), 500 mg/d C1: Placebo, 500 mg/d | 12 w | 20 | 16 | I1:54.17 ± 13.60 C1: 61.50 ± 8.68 |

(Continued)

TABLE 1 Continued

| Study | Country | Sample | | RCT design (blinding) | Patient | Intervention | During | Sex | | Age |
|-----------------------|---------|--------|----|--|---------|--|--------|-----|----|---------------------------------------|
| | | I | C | | | | | M | F | |
| Soleimani et al. (27) | Iran | 30 | 30 | Randomized double-blind placebo-controlled parallel clinical trial | HD | I1: Probiotic capsule (L. acidophilus, L casei and B. bifidum)2 10 ⁹ CFU/g/d C1: Placebo | 12 w | 40 | 20 | I1: 54 ± 16 C1: 59.4 ± 16 |
| Wang et al. (24) | China | 21 | 18 | Randomized, double-blind, placebo-controlled trial | PD | I1: Probiotic capsule, 90 billion CFU/day C1: Placebo capsule(maltodextrin) | 24 w | 18 | 21 | I1: 51 ± 11.33 C1: 53.5 ± 11.85 |
| Borges et al. (28) | Brazil | 16 | 17 | Randomized, double-blind, placebo-controlled trial | HD | I1: Probiotic capsule (30 billion live bacteria, totaling 90 billion colony-forming units (CFU)/d, included Streptococcus thermophilus, Lactobacillus acidophilus, and Bifidobacterial longum), 3 capsules/d C1: Placebo capsule, 3 capsules/d | 12 w | 21 | 12 | I1: 53.6 ± 11.0 C1: 50.3 ± 8.5 |
| Liu et al. (37) | China | 22 | 23 | Randomized double-blind placebo trial | HD | I1: Probiotic capsule (2.2 × 10 ⁹ cfu Balonium NQ1501, 0.53 × 10 ⁹ cfu.L. acidophilus YIT2004, and 1.1 × 10 ⁹ cfu E. faecalis YIT0072),8 capsule/d C1: Placebo capsules (pregelatinized starch and lactose), 8 capsule/d | 24 w | 23 | 22 | I1:49 ± 9 C1:48 ± 11 |
| Pan et al. (42) | China | 50 | 48 | Randomized controlled trial | PD | I1: Probiotic capsules (Bifidobacterium longum, Lactobacillus bulgaricus, and Streptococcus thermophilus), 6 capsules/d C1: Maltodextrin capsules, 6 capsules/d | 8 w | 56 | 42 | I1: 49.31 ± 13.13 C1:50.92 ± 17.60 |
| Natarajan et al. (21) | America | 19 | 18 | Randomized, double-blind, placebo-controlled crossover trial | HD | I1: Probiotic capsule (30 billion CFU of S. thermophilus KB 19, L. acidophilus KB 27, and B. longum KB 31), 6 capsules/d C1: Placebo capsules (a 1:1 blend of cream of wheat and psyllium husk)/d | 24 w | 6 | 16 | I1:54 ± 39.62 C1:NA |
| Eidi et al. (29) | Iran | 21 | 21 | Randomized triple-blind placebo-controlled trial | HD | I1: Probiotic capsule (1.6 × 10 ⁷ CFU of Lactobacillus Rhamnoses), one capsule/d C1: Placebo capsule, one capsule/d | 4 w | 32 | 10 | I1: 57.05 ± 13.95 C1:59.67 ± 15.04 |
| Soleimani et al. (15) | Iran | 30 | 30 | Randomized, double-blind, placebo-controlled clinical trial | HD | I1: Synbiotic capsule (Lactobacillus acidophilus, Lactobacillus casei, and Bifidobacterium bifidum (2 × 10 ⁹ CFU/day each) plus 0.8 g/day of inulin) C1: Placebo (corn starch) | 12 w | 42 | 18 | I1: 62.8 ± 12.7 C1: 62.8 ± 14.8 |

(Continued)

TABLE 1 Continued

| Study | Country | Sample | | RCT design (blinding) | Patient | Intervention | During | Sex | | Age |
|-------------------------------|---------|--------|-------|--|---------|--|--------|-----|----|---|
| | | I | C | | | | | M | F | |
| Viramontes-Horner et al. (23) | Mexico | 20 | 15 | Randomized double-blind, placebo-controlled, clinical trial | HD | I1: Symbiotic gel (Nutrihealth, Nutriments Inteligentes, S.A. de C.V. Guadalajara, Jalisco, Mexico) contained a mix of probiotics and 2.31 g of a prebiotic fiber (inulin); 1.5 g of omega-3 fatty acids and vitamins), 14 gels/d C1: Placebo, 14 gels/d | 8 w | 32 | 10 | I1: 40.6 ± 17.1 C1: 39.0 ± 16.0 |
| Lopes et al. (35) | Brazil | 29 | 29 | Randomized, simple-blind, placebo-controlled trial | HD | I1: Synbiotic drink (100 ml probiotic and 40 g of extruded sorghum flakes) C1: Placebo drink (100 mL of pasteurized milk and 40 g of extruded corn flakes) | 7 w | 38 | 20 | I1: 63.17 ± 11.16 C1: 63.03 ± 10.77 |
| Haghighat et al. (31) | Iran | 11:23 | 12:23 | Randomized, double-blind, parallel group, placebo-controlled trial | HD | I1: Synbiotic sachet (5 g probiotics and 15 g of prebiotics), 20 g/d I2: Probiotic powder (5 g probiotics and 15 g of maltodextrin powder), 20 g/d C1: Maltodextrin powder, 20 g/d | 12 w | 34 | 31 | I1: 48.04 ± 10.11 I2: 46.21 ± 11.49 C1: 45.47 ± 10.76 |
| Kooshki et al. (33) | Iran | 23 | 23 | Randomized, double-blind, placebo-controlled trial | HD | I1: Synbiotic capsules (100 mg of lactol probiotic, which contains Lactobacillus coagulans and fructo-oligosaccharides), 2 capsules/d C1: Placebo capsules (farina), 2 capsules/d | 8 w | 21 | 25 | I1: 62.92 ± 16.80 C1: 62.83 ± 16.62 |
| Cruz-Mora et al. (20) | Mexico | 8 | 10 | Randomized, double-blind, placebo-controlled clinical trial | HD | I1: Symbiotic gel (probiotic of 2.0×10^{12} colony-forming units; 2.31 g of a prebiotic fiber (inulin); 1.5 g of omega-3 fatty acids (eicosatetraenoic and docosahexaenoic acid) and vitamins (complex B, folic acid, ascorbic acid, and vitamin E) C1: Placebo gel (a gel without prebiotic fiber, probiotics, omega-3 fatty acids, vitamins) | 8 w | 15 | 3 | I1: 34 ± 10 C1: 30.6 ± 9.5 |
| Mirzaeian et al. (38) | Iran | 21 | 21 | Randomized, double-blind, placebo-controlled clinical trial | HD | I1: Synbiotic capsule (Lactobacillus casei L. acidophilus Rhamnoses, Bulgaricus, Bifidobacterium breve, B. longum and Streptococcus thermophiles and fructo-oligosaccharide as prebiotic in addition to lactose, magnesium stearate, and talc as filling materials), 1 g/d C1: Placebo capsules (maltodextrin), 1 g/d | 8 w | 30 | 12 | I1: 58.30 ± 11.3 C1: 69.74 ± 42.87 |

I, intervention; C, control; RCT, randomized clinical trial; HD, hemodialysis; PD, peritoneal dialysis; M, male; F, female; W, week; NA, not available.

to **Discussion**, Paragraph 3. The corrected sentence appears below:

“Prebiotics were superior in reducing serum IS, prebiotics were rated as best in reducing MDA level. The accumulation of metabolic toxins in the blood is closely associated with the deteriorating progression of CKD to ESRD, part of the toxins, such as protein-bound uremic toxins, come from intestinal flora, and dialysis is not potentially removed (9, 45). The efficacy of pro/pre/syn-biotics in lowering uremic toxins has been demonstrated by previous meta-analysis (13, 49). Our pairwise comparison found the same results and notably we further suggested that prebiotics and synbiotics are the most effective supplements. Prebiotics are some non-digestible food ingredients, regarded as a vital dietary supplement for ESRD patients with dietary restriction of protein intake, increasing the concentration of short-chain fatty acids (SCFAs), which benefit metabolites produced by gut bacterium (12, 50). Decreased SCFAs were regarded as one of the main mechanisms of the production of uremic toxins, which may also be the reason why prebiotics were more effective than probiotics and synbiotics. MDA is a low-molecular-weight solution that participates in oxidative stress, connecting with the progress of CKD and its cardiovascular complications (51). Seven randomized controlled trials were introduced in the study of Nguyen et al. (14), who found that MDA was significantly reduced in hemodialysis patients after taking three supplements. Several studies also have

demonstrated that synbiotics might increase the expression of the antioxidant gene SOD and GPX in the gut by targeting gut bacteria to activate oxidative stability (52, 53). Current studies support the evidence that taking prebiotics and synbiotics have the most beneficial influence in reducing IS and MDA. Whereas, it is of great importance to emphasize that the change of uremic toxins is the result of multiple comparisons among the three drugs, combining small samples of studies and different follow-up times, which declined the strength of evidence, contributing to the accuracy of evidence is low. Thus, launching large clinical trials is important to evaluate the function of pro/pre/syn-biotics in reducing uremic toxins, especially protein-bound uremic toxins.”

The authors apologize for these errors and state that this does not change the scientific conclusions of the article in any way. The original article has been updated.

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