RESEARCH ARTICLE

Nutritional Status in Nocturnal Hemodialysis Patients – A Systematic Review with Meta-Analysis

Karin J. R. Ipema[1,2]*, Simone Struijk[2], Annet van der Velden[2], Ralf Westerhuis[1,3], Cees P. van der Schans[2,4], Carlo A. J. M. Gaillard[3], Wim P. Krijnen[2], Casper F. M. Franssen[3]

1 Dialysis Center Groningen, Groningen, The Netherlands, 2 Research group Healthy Ageing, Allied Health Care and Nursing, Hanze University Groningen, University of Applied Sciences, Groningen, the Netherlands, 3 Department of Internal Medicine, Division of Nephrology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands, 4 Department of Rehabilitation Medicine, Center for Rehabilitation, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

* k.ipema@dcg.nl

Abstract

Background

Hemodialysis patients experience an elevated risk of malnutrition associated with increased morbidity and mortality. Nocturnal hemodialysis (NHD) results in more effective removal of waste products and fluids. Therefore, diet and fluid restrictions are less restricted in NHD patients. However, it is ambiguous whether transition from conventional hemodialysis (CHD) to NHD leads to improved intake and nutritional status. We studied the effect of NHD on protein intake, laboratory indices of nutritional status, and body composition.

Study design

Systematic review with meta-analysis.

Population

NHD patients.

Search strategy

Systematic literature search from databases, Medline, Cinahl, EMBASE and The Cochrane Library, to identify studies reporting on nutritional status post-transition from CHD to NHD.

Intervention

Transition from CHD to NHD.

Outcomes

Albumin, normalized protein catabolic rate (nPCR), dry body weight (DBW), body mass index (BMI), phase angle, protein intake, and energy intake.

Results

Systematic literature search revealed 13 studies comprising 282 patients that made the transition from CHD to NHD. Meta-analysis included nine studies in 229 patients. In control group controlled studies (n = 4), serum albumin increased significantly from baseline to 4–6 months in NHD patients compared with patients that remained on CHD (mean difference 1.3 g/l, 95% CI 0.02; 2.58, p = 0.05). In baseline controlled studies, from baseline to 4–6 months of NHD treatment, significant increases were ascertained in serum albumin (mean difference (MD) 1.63 g/l, 95% CI 0.73–2.53, p<0.001); nPCR (MD 0.16 g/kg/day; 95% CI 0.04–0.29, p = 0.01); protein intake (MD 18.9 g, 95% CI 9.7–28.2, p<0.001); and energy intake (MD 183.2 kcal, 95% CI 16.8–349.7, p = 0.03). Homogeneity was rejected only for nPCR (baseline versus 4–6 months). DBW, BMI, and phase angle did not significantly change. Similar results were obtained for comparison between baseline and 8–12 months of NHD treatment.

Limitations

Most studies had moderate sample sizes; some had incomplete dietary records and relatively brief follow-up period. Studies markedly differed with regard to study design.

Conclusions

NHD is associated with significantly higher protein and energy intake as well as increases in serum albumin and nPCR. However, the data on body composition are inconclusive.

Introduction

Malnutrition is a frequent problem experienced by hemodialysis patients and forms one of the primary causes of the high morbidity and mortality in this patient group [1,2]. Various factors contribute to malnutrition in patients with end-stage renal disease, e.g., increased protein and energy requirements [3], reduced appetite and food-intake [1,4,5], protein-energy wasting as a result of chronic inflammation [6,7], and reduced physical activity [8]. Frequent nocturnal home hemodialysis (NHHD) is the dialysis treatment with the greatest weekly removal of uremic toxins. Nocturnal in-centre hemodialysis (NCHD) is an alternative for patients who are not applicable for home hemodialysis and have medical and/or social reasons for nocturnal or more efficient hemodialysis.

According to several studies, prolonged hemodialysis sessions, either at home or in-center, may improve clinical outcomes [9–11]. A hemodialysis schedule of three times per week of eight hours improved nutritional status, volume status, and survival rates [12]. Nocturnal hemodialysis (NHD) combines the long duration dialysis and more frequent treatments which results in ameliorated elimination of waste products and fluids. Therefore, diet and fluid restrictions are usually less stringent in NHD patients compared with patients on conventional hemodialysis (CHD). NHD patients use significantly less or no phosphate binders which may result in a revitalized appetite [13,14]. Receiving dialysis during the night may also facilitate a more 'normal' day rhythm with less disturbances of eating patterns. All of these factors may modify the pattern of food consumption after the transition from CHD to NHD.

Current knowledge regarding long-term effects of NHD on nutritional status is limited. Therefore, we performed a systematic review on the effect on nutritional status with the transition from CHD to NHD. We specifically studied the effect of NHD on protein intake, laboratory indices of nutritional status, and body composition.

Methods

Study protocol and information sources

This systematic review was performed between October 3rd, 2013, and February 1st, 2014, from databases of Medline, Cinahl, EMBASE, and the Cochrane Library, according study protocol (S1 File). We followed the PRISMA recommendations for reporting data and meta-analysis (PRISMA 2009) (S1 Table).

Eligibility criteria

Studies were eligible for inclusion if the following criteria were satisfied: (1) nocturnal hemodialysis administered to adults (aged ≥18 years) experiencing chronic kidney disease; (2) outcomes of interest are scores relating to the patients nutritional status; and (3) full-length articles published between January 1st, 1990, and February 1st, 2014, and written in English. Data was required to be obtained by original research and not from reviews. Due to an expected minimal number of randomized controlled trials (RCT's), there was no exclusion criterion based upon methodology applied to the studies. The selection procedure included RCT's, controlled trials, cohort studies including observational studies with a comparison group, case-control studies, and prospective longitudinal studies comparing nutritional parameters prior to and following the transition from CHD to NHD.

Search strategy

Different combinations of terms and 'strings' were exploited in order to examine the effects of the search strategy. The search strategy for Medline is detailed in Table 1.

Study selection and data collection

Two reviewers (SS and AV) separately screened the titles and abstracts of the studies that were identified through electronic searching in order to select those that were potentially eligible for inclusion. Additional studies were identified through the references of the pertinent studies. After the screening, the reviewers discussed any variances in the study selection. Studies were determined as definitely eligible for inclusion if outcomes were available for laboratory measurements, food intake, or body composition in NHD patients. Study details (publication year, study design, patients' characteristics, interventions, and outcomes) were aggregated in a standard spreadsheet (Microsoft Corporation, Redmond, Washington, USA) for summary and analyses.

Risk of bias and quality assessment

All full-text versions of potentially relevant studies were independently screened by three reviewers (SS, AV, KI) to identify whether studies were definitely eligible for inclusion and to assess their quality. Study quality was assessed by employing the Newcastle-Ottawa Scale for cohort studies [15]. The scale consists of three quality criteria: selection, comparability, and outcome. The maximal score is 9 points (4 for selection, 2 for comparability, and 3 for outcome). Study quality was defined as poor when the score was 1–3, fair when the score was 4–6, and good when the score was 7–9 points.

Table 1. Search strategy for Medline.

To locate hemodialysis:
1. Renal Dialysis [Mesh:noexp]
2. Hemodialysis, Home [Mesh]
3. Hemodialysis* [tw]
4. Haemodialysis*[tw]
5. Or/1-4
To locate Nocturnal
6. Nocturnal [tw]
7. Night* [tw]
8. Or/6-7
To locate Nutritional status
9. Malnutrition [Mesh]
10. Nutritional Physiological Phenomena [Mesh]
11. Body weights and Measures [Mesh]
12. Nutrition [tw]
13. Food* [tw]
14. Protein [tw]
15. Proteins [tw]
16. Energy [tw]
17. Body composition [tw]
18. Or/9-17
19. 5 and 8 and 18

doi:10.1371/journal.pone.0157621.t001

Data extraction

Information was collected of study designs, participant details, exclusion and inclusion criteria, interventions, and any comparators and outcomes. The following variables were selected after a pilot search and included as outcome variables: dry body weight, pre-dialysis weight, post-dialysis weight, dry lean body mass, interdialytic weight gain, fat mass, body mass index (BMI), body cell mass (BCM), extracellular mass (ECM), extracellular water (ECW), intracellular water (ICW), energy intake, protein intake, carbohydrate intake, fat intake, albumin levels, (normalized) protein catabolic rate ((n)PCR), (normalized) protein nitrogen appearance ((n)PNA), C-Reactive protein (CRP), bioimpedance phase angle, mid upper arm muscle circumference (MUAMC), arm muscle area.

Statistical analyses

To assess differences in nutritional parameters, albumin, nPCR, dry body weight, BMI, phase angle, protein intake, and energy intake between baseline (on CHD) and, after a certain duration on NHD, a meta-analysis with a calculation of the mean differences with a 95% confidence interval was performed utilizing statistical programming language R (R Development Core Team (2014). There were two types of studies: 'baseline controlled studies' in which parameters at baseline and after a certain period on NHD were compared and 'control group controlled' studies that compared patients who made the transition from CHD to NHD with a control-group of patients that remained on CHD. For meta-analyses, data from baseline controlled and the NHD-arm of control group controlled studies were pooled whenever possible. To assess the differences in albumin between the NHD group and the control group, we also performed

a meta-analysis (other nutritional parameters were assessed in too few control group controlled studies), with a calculation of the differences in mean with a 95% confidence interval.

Meta-analyses were conducted when the results of this parameter were available in three or more studies. Studies varied during the intervals wherein nutritional parameters were assessed after the transition from CHD to NHD. For surveying feasibility, we combined assessments for 4 to 6 months and for 8 to 12 months following the transition. The weights of the meta-analyses were based on the inverse variance method; the heterogeneity parameter (Tau^2) for effect size was based on restricted maximum-likelihood. The random effects model was selected for the mean difference because an omnipresent treatment effect not being identical in size across all of the studies was expected [16]. Forest plots were constructed to summarize the outcome of the meta-analyses.

Characteristics of the NHD patients and the control groups as described in the studies were reported as mean±SD. One study reported the standard error (SE) as opposed to standard deviation (SD) [14]. The original data were kindly provided to us by the authors and, consecutively, the SD was calculated from the SE and the number of patients (n) as SD = SE$^*\sqrt{n}$. One study had two research groups receiving nocturnal HD; one group dialyzed three times per week, and the other group dialyzed six times per week [17]. The data of these two research groups were included separately in the meta-analysis. In the meta-analysis for the comparison of NHD patients and controls, we primarily included the NHD group that dialyzed six times per week. In a separate analysis, we also performed the meta-analyses employing the NHD group that dialyzed three times per week instead of the group that dialyzed six times per week. This study incorporated two control groups with day-time hemodialysis: one group receiving dialysis three times per week for 2.5 to 4.0 hours and one group having dialysis six times per week for 1.5 to 2.75 hours. In our analyses, we only used the control group of three times per week HD because this dialysis schedule was most appropriately comparable with other studies.

Kaysen et al reported the ePCR while the majority of the other studies reported the nPCR [17]. Upon our request, the authors provided the results of the nPCR [17]. Since one study did not report the results of (the change in) dry body weight in the text, these results were estimated from the figure [18].

An influence analysis was a component of each meta-analysis to check whether the conclusion critically depends upon the results of a single study. A test for funnel plot asymmetry based on the linear regression method was added to indicate any risk of bias. Only funnel plots containing outlying studies are shown in order to save space. P-values <0.05 were considered statistically significant.

Results

Search results

The literature search yielded a total of 563 articles: 156 in Medline, 300 in EMBASE, 40 in Cinahl, and 67 in the Cochrane Library. After screening the titles (of these 563 articles) 159 manuscripts and 9 references remained from other sources such as searching citations and examination of reference lists from relevant studies. After eliminating the duplicates, 89 records remained. The abstracts of these articles were screened by 3 reviewers (SS, AV, KI). A total of 28 full-text articles were assessed for eligibility after which 15 full-text articles were excluded as they did not meet the inclusion criteria for original research [19–25] or for other reasons, e.g., the focus on phosphate control [26–29], survival [10,30], dialysis efficiency [31], and left ventricular mass [32]. Finally, 13 studies were included for this systematic review (Fig 1). Of these, four studies were excluded from meta-analysis for different reasons. In one study, merely five participants were studied with an observation period of only eight weeks [33], in
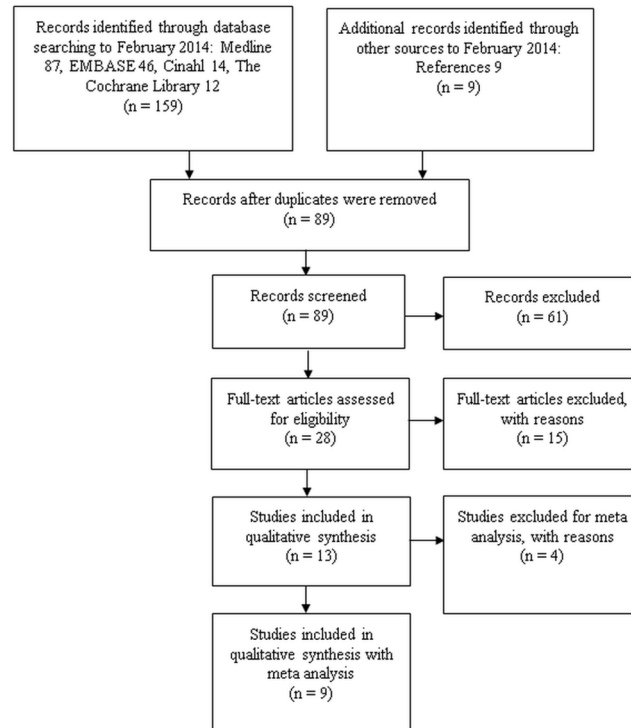
Fig 1. Selection of articles for the systematic review on nutritional status in NHD patients.

doi:10.1371/journal.pone.0157621.g001

one study, no SD's were available [34]; in another study, the duration on NHD was not clearly stated [35]. An additional study was excluded because nocturnal hemodialysis was performed with online hemodiafiltration [36]. The remaining nine studies incorporated data on one or more nutritional parameters, and these studies were included in the meta-analysis of the effect of nocturnal hemodialysis on nutritional status (Fig 1).

Study designs, characteristics, and participants

Table 2 indicates study designs, study characteristics, information on participants, and study quality. Detailed results of biochemical nutritional parameters, body composition, and food records are summarized in S2 Table.

Three studies excluded patients that had severe co-morbid conditions (for example, patients with diabetes mellitus, documented cancer, dementia, cardiac angina during the two week period prior to the study, active infections) and other relevant conditions such as secondary hyperparathyroidism with need of calcium-sensitizing therapy, central venous catheter, required erythrocyte transfusion, severe arterial hypertension, technical reasons, having pacemakers, or amputation of a major limb [33,37,38]. In another study, an average creatinine and urea clearance >10 ml/min/1.73m^2 were exclusion criteria [17]. In certain studies, short life expectancy [39], inappropriate housing and inability to speak English [40], lacking the physical ability or cognitive function to train for NHD [41], as well as the absence of a partner to assist with in-home NHD [14] were reasons for exclusion. Five studies described no specific exclusion criteria [18,34–36,42]. Major inclusion criteria in all studies were the receptiveness to participate and the capability to be trained for NHD.

Inclusively, in all 13 studies, 282 patients made the transition from CHD to NHD. Four of these 13 studies (comprising 168 patients on NHD) had a control group of CHD patients (208

Table 2. Summary of characteristics studies.

Author	Duration of studies (months)	No. NHD patients	Men (n)	Mean age (years) mean±SD	In-centre /home NHD	Duration of NHD treatment	Study design	Single centre y/n	Control group y/n	Meta analysisy/n	Study quality
Alloatti,2002	>6	13	12 (92.3%)	52.0±13.0	In-centre	3 times/week for 8 hours	prospective	Y	N	N	4
Cravedi,2009	24	7	6 (85.7%)	50.4±11.0	In-centre	3 times/week for 8 hours	retrospective	Y	N	Y	5
David,2009	12	13	11 (84.6%)	34.8±13.7	In-centre	3 times/week for 8 hours	prospectivelongitudinal	Y	N	Y	5
Demirci,2013	12	57	41 (71.9%)	47.1±11.7	In-centre	3 times/week for 8 hours	prospective cohort trial	N	Y	Y	7
Ipema,2012	8	15	11 (73.3%)	53.4±10.3	Home	5/6 times/week for 8 hours	prospective observational	Y	N	Y	5
Kaysen,2012	12	87	57 (65.5%)		Home		prospective randomized trial	N	Y	Y	8
		42	28 (66.7%)	54.0±12.9		3 times/ week $\geq$ 2.5 hours					
		45	29 (64.4%)	51.7±14.4		6 times/ week $\geq$ 6 hours					
Maduel,2011	12	26	18 (69.2%)	49.2±14.0	In-centre		crossover prospective	Y	N	N	8
McPhatter,1999	18	11	5 (45.5%)	50.0±na	Home	5–6 times/week for 4–9 hours	prospectiveobservational	Y	N	N	5
O'Sullivan, 1998	2	5	3 (60%)	46,6±na	In-centre	6 times/week for 8 hours	pilot study	Y	N	N	3
Pierratos,1997	36	11	8 (72.7%)	40±10.0	Home	6–7 times/week for 8–10 hours	prospective	Y	N	Y	5
Schorr,2011	6	12	6 (50%)	54,2±13.0	Home	5–6 times/week for$\geq$ 6 hours	randomized trial	Y	Y	Y	7
Sikkes,2009	12	14	13 (92.9%)	47.0±7.8	Home	6 times/week for 8 hours	prospective non-randomized	Y	N	Y	5
Spanner,2003	18	13	10 (76.9%)	44,2±6.4	Home	5–6 times/week for 6–8 hours	prospective controlled non-randomized	N	Y	Y	7

Abbreviations: NHD: nocturnal hemodialysis.

doi:10.1371/journal.pone.0157621.t002

patients on CHD) [17,37,41,42]. The other nine studies (comprising 114 NHD patients) compared their outcomes to measurements at baseline prior to patients beginning NHD [14,18,33–36,38–40]. The length of the intervention period on NHD ranged between eight weeks and three years.

The score on the Newcastle Ottawa Scale for cohort studies ranged from 3 to 8, one study was considered poor [33], seven were considered fair [14,18,34,35,38–40], and five were considered good [17,36,37,41,42]. There were no randomized controlled trials.

Biochemical nutritional measurements

Control group controlled studies. Serum albumin was measured in 12 studies. A meta-analysis comparing NHD patients and control patients that remained on CHD is performed on the results from four studies. A meta-analysis for the comparison of albumin levels at baseline (before the transition from CHD to NHD) between NHD patients and CHD patients demonstrated no differences (mean difference -0.1 g/l, 95% CI -0.82; 0.61, P = 0.78) (Fig 2a). Influence analyses and funnel plot indicated no bias (data not shown). The meta-analysis of the comparison of the means of three studies that compared NHD patients with a follow up period of 4–6 months with control patients that continued on CHD for 4–6 months showed a
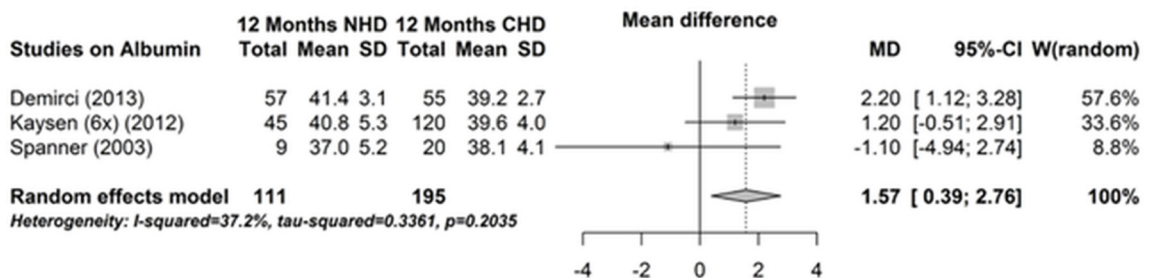
2a
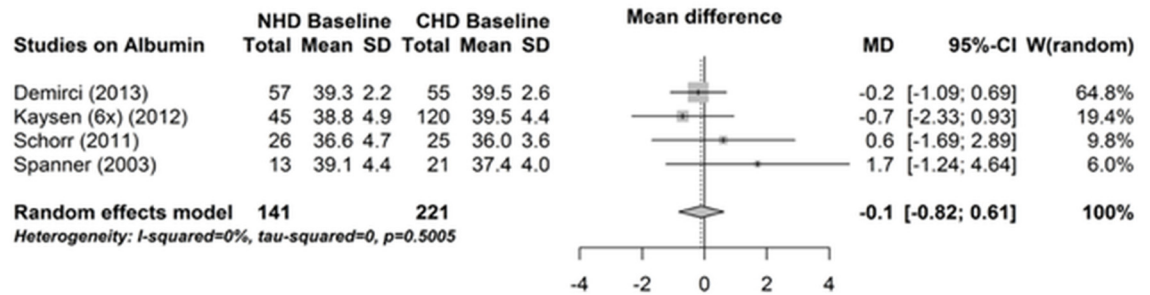
2b
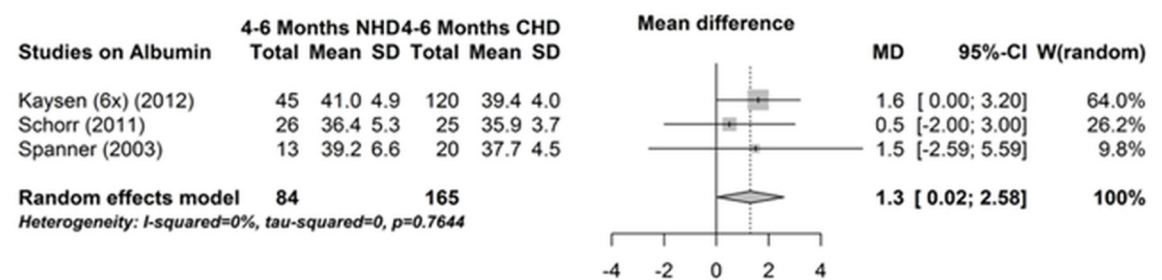
2c

Fig 2. Albumin—control group controlled studies. (2a) Forest plot comparing albumin in NHD patients at baseline (before transition from CHD to NHD) and control CHD patients. (2b) Forest plot comparing albumin in NHD patients after 4–6 months on NHD and control CHD patients after 4–6 months follow up. (2c) Forest plot comparing albumin in NHD patients after 12 months on NHD and control CHD patients after 12 months follow up.

doi:10.1371/journal.pone.0157621.g002

borderline significant increase in serum albumin in NHD patients (mean difference 1.3 g/l, 95% CI 0.02; 2.58, P = 0.05) (Fig 2b). The influence analysis shows a modification in the results after removing one particular study (Table 3). The funnel plot indicated no bias (data not shown). The meta-analysis comparing NHD patients at 12 months following the transition compared with control patients after 12 months of follow-up also indicated a significant increase in serum albumin (mean difference 1.57 g/l, 95% CI 0.39; 2.76, P = 0.01) (Fig 2c). The influence analysis showed a change in the results after omitting a particular study (Table 4). The funnel plot indicated no bias (data not shown).

Identical results were obtained when the meta-analysis comparing albumin levels between NHD and CHD control patients was performed with the NHD group that dialyzed three times

Table 3. Influence analysis of albumin at 4–6 months of NHD versus controls on CHD.

	Mean difference	95% confidence interval	P-value
Omitting Kaysen (6x per week) (2012)	0.77	-1.36–2.91	0.479
Omitting Schorr (2011)	1.59	0.10–3.08	0.037
Omitting Spanner (2003)	1.28	-0.07–2.63	0.063
Pooled estimate	1.30	0.02–2.58	0.046

doi:10.1371/journal.pone.0157621.t003

per week instead of the NHD group that dialyzed six times per week NHD (S1A, S1B and S1C Fig).

Baseline controlled studies. The results of eight baseline controlled studies on albumin are exploited in a meta-analysis. Serum albumin significantly increased from baseline to 4–6 months NHD (mean difference 1.63 g/l, 95% CI 0.73; 2.53, P<0.001) (Fig 3a) and from baseline to 8–12 months NHD (mean difference 1.79 g/l, 95% CI 1.14; 2.45, P<0.001) (Fig 3b). Influence analysis and funnel plots indicated no bias (data not shown).

Nine studies reported results on nPCR whereby six could be utilized in the meta-analysis. As illustrated in Fig 4a, nPCR significantly improved from baseline to 4–6 months on NHD (mean difference 0.16 g/kg/day, 95% CI 0.04; 0.29, P = 0.01). The homogeneity of effects was rejected in this meta-analysis by a p-value of 0.005. A test for funnel plot asymmetry revealed that two studies fell outside the broken lines of the funnel plot in the comparison of nPCR between baseline and 4–6 months [14,17] (Fig 4c). The influence analysis showed no changes after the omission of any single study. The nPCR also significantly improved from baseline to 8–12 months NHD (mean difference 0.15 g/kg/day, 95% CI 0.09; 0.22, P<0.001) (Fig 4b). In this analysis, the homogeneity of the effects was not rejected (P = 0.35). There was neither an outlying study from the funnel plot nor an influential study after omitting a single study.

CRP was measured in three studies [36–38]. Meta-analysis was not performed since only two of these studies were appropriate for this analysis. In two studies, CRP did not significantly differ between baseline and 12 months on NHD [36,38] whereas, in another study, CRP decreased significantly from baseline to 12 months on NHD [37]. In the latter study, the course of CRP values did not differ between the NHD group and the control group over the course of one year [37].

Body composition

All thirteen studies reported data on the course of body weight. Six of these studies could be employed for the meta-analysis (Fig 5). Dry (post-dialysis) body weight did not change from baseline to 4–6 months NHD (mean difference 0.28 kg, 95% CI -4.32; 4.88, P = 0.9) (Fig 5a) and from baseline to 8–12 months NHD (mean difference 1.62 kg, 95% CI -3.70; 6.95, P = 0.55) (Fig 5b). Influence analyses and funnel plot indicated no bias (data not shown).

Five studies reported data on BMI. As depicted in Fig 6, BMI did not change from baseline to 4–6 months (mean difference 0.37, 95% CI -1.36; 2.09, P = 0.68) (Fig 6a) and from baseline

Table 4. Influence analysis of albumin at 12 months of NHD versus controls CHD.

	Mean difference	95% confidence interval	P-value
Omitting Demirci (2013)	0.72	-1.11–2.55	0.44
Omitting Kaysen (6x per week) (2012)	1.09	-1.97–4.14	0.486
Omitting Spanner (2003)	1.92	1.01–2.83	0.000
Pooled estimate	1.57	0.39–2.76	0.009

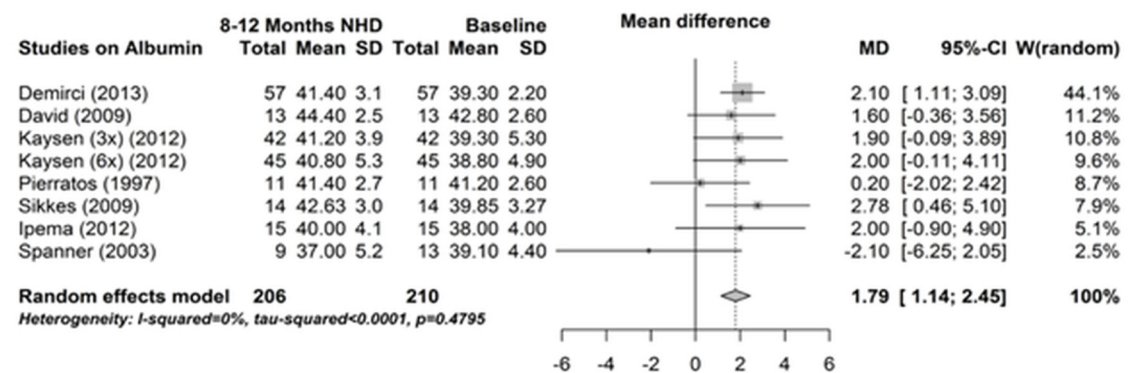doi:10.1371/journal.pone.0157621.t004

3a
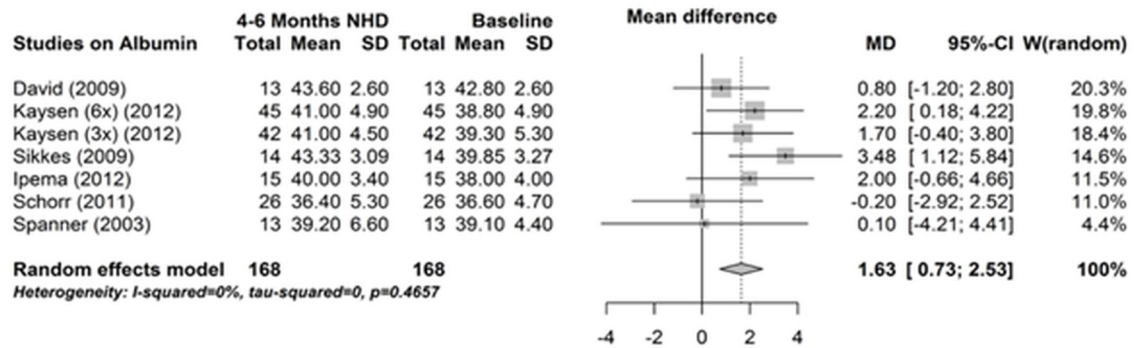
3b

Fig 3. Albumin—baseline controlled studies. (3a) Forest plot comparing albumin in NHD patients at baseline (before beginning NHD) and after 4–6 months on NHD. (3b) Forest plot comparing albumin in NHD patients at baseline (before beginning NHD) and after 8–12 months on NHD.

doi:10.1371/journal.pone.0157621.g003

to 8–12 months (mean difference 0.98, 95% CI -0.99; 2.95, P = 0.33) (Fig 6b). Influence analyses and funnel plot indicated no bias (data not shown).
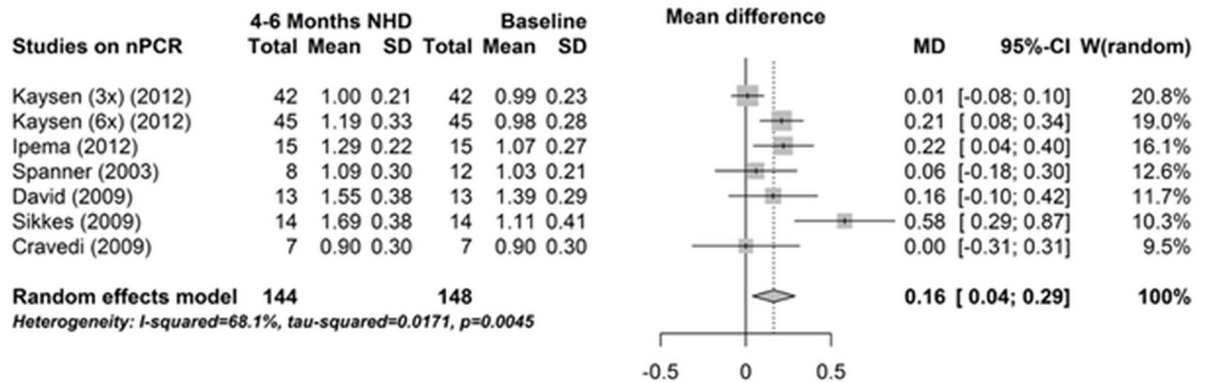
Lean body mass measured with bioimpedance analysis (BIA) was reported in two studies. One indicated a significant increase in lean body mass compared with the CHD control group after 12 months [37]. The other showed no significant change in lean body mass during an observation period of 12 months [17].

ECW, ICW, ECM, and BCM were measured with BIA in three studies. One study reported significant decreases in ECW normalized for weight and in ECW normalized for height after 12 months of follow-up compared with the control group [37]. Another study documented that the ratio of the ECM and BCM (ECM/BCM) decreased significantly from baseline to 12 months on NHD [38]. The third and largest study reported no significant changes in ECW, ICW, and total body water in NHD patients during 12 months of follow-up [17]. Meta-analysis was not performed because these studies used different outcome parameters.
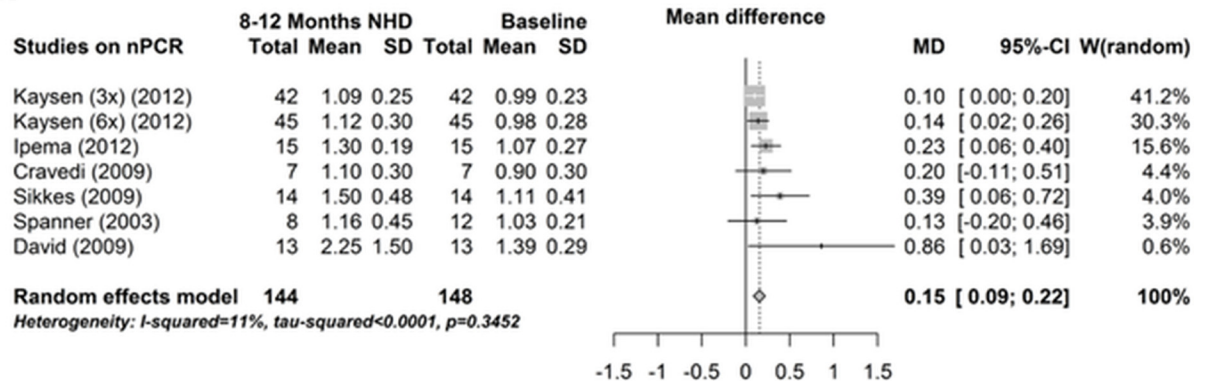
Interdialytic weight was reported in two studies. One showed a significant increase from baseline to 8 months NHD [39] while the other indicated no change between baseline and 12 months of NHD [36].

Three studies measured fat mass. One study denoted a significant increase after 12 months on NHD compared with the control group [37]. Another study reported no significant change

4a

Studies on nPCR	4-6 Months NHD			Baseline			Mean difference	MD	95%-CI	W(random)
	Total	Mean	SD	Total	Mean	SD				
Kaysen (3x) (2012)	42	1.00	0.21	42	0.99	0.23		0.01	[-0.08; 0.10]	20.8%
Kaysen (6x) (2012)	45	1.19	0.33	45	0.98	0.28		0.21	[0.08; 0.34]	19.0%
Ipema (2012)	15	1.29	0.22	15	1.07	0.27		0.22	[0.04; 0.40]	16.1%
Spanner (2003)	8	1.09	0.30	12	1.03	0.21		0.06	[-0.18; 0.30]	12.6%
David (2009)	13	1.55	0.38	13	1.39	0.29		0.16	[-0.10; 0.42]	11.7%
Sikkes (2009)	14	1.69	0.38	14	1.11	0.41		0.58	[0.29; 0.87]	10.3%
Cravedi (2009)	7	0.90	0.30	7	0.90	0.30		0.00	[-0.31; 0.31]	9.5%
Random effects model	144			148				0.16	[0.04; 0.29]	100%

Heterogeneity: I-squared=68.1%, tau-squared=0.0171, p=0.0045

4b

Studies on nPCR	8-12 Months NHD			Baseline			Mean difference	MD	95%-CI	W(random)
	Total	Mean	SD	Total	Mean	SD				
Kaysen (3x) (2012)	42	1.09	0.25	42	0.99	0.23		0.10	[0.00; 0.20]	41.2%
Kaysen (6x) (2012)	45	1.12	0.30	45	0.98	0.28		0.14	[0.02; 0.26]	30.3%
Ipema (2012)	15	1.30	0.19	15	1.07	0.27		0.23	[0.06; 0.40]	15.6%
Cravedi (2009)	7	1.10	0.30	7	0.90	0.30		0.20	[-0.11; 0.51]	4.4%
Sikkes (2009)	14	1.50	0.48	14	1.11	0.41		0.39	[0.06; 0.72]	4.0%
Spanner (2003)	8	1.16	0.45	12	1.03	0.21		0.13	[-0.20; 0.46]	3.9%
David (2009)	13	2.25	1.50	13	1.39	0.29		0.86	[0.03; 1.69]	0.6%
Random effects model	144			148				0.15	[0.09; 0.22]	100%

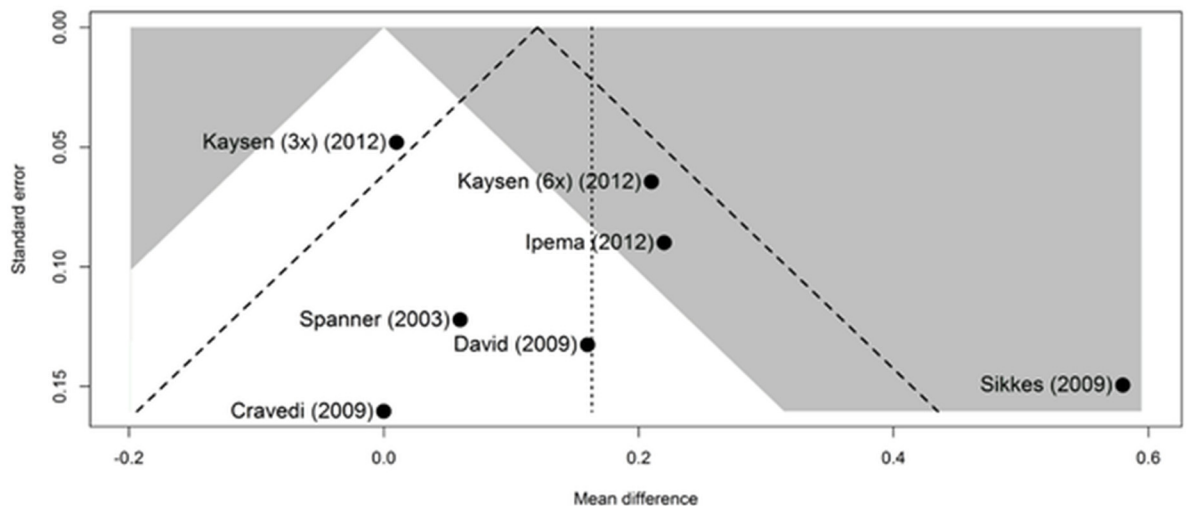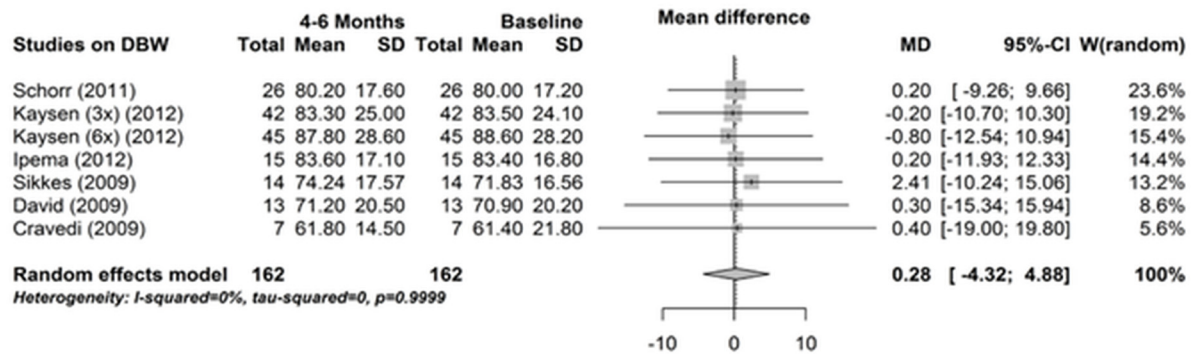Heterogeneity: I-squared=11%, tau-squared<0.0001, p=0.3452

4c

Fig 4. normalized Protein Catabolic Rate. (4a) Forest plot comparing nPCR in NHD patients at baseline (prior to beginning NHD) and after 4–6 months on NHD. (4b) Forest plot comparing nPCR in NHD patients at baseline (prior to beginning NHD) and after 8–12 months on NHD. (4c) Funnel plot comparing nPCR in NHD patients at baseline (prior to beginning NHD) and after 4–6 months on NHD.
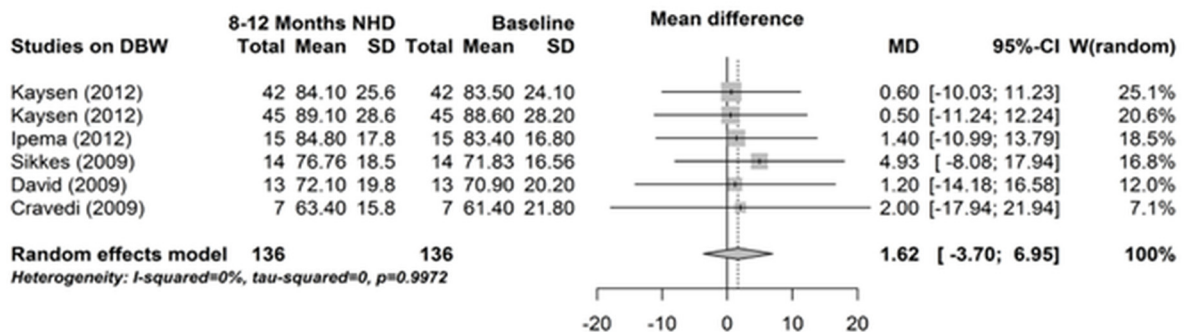
doi:10.1371/journal.pone.0157621.g004

5a

Studies on DBW	4-6 Months Total Mean SD	Baseline Total Mean SD	Mean difference	MD	95%-CI	W(random)
Schorr (2011)	26 80.20 17.60	26 80.00 17.20		0.20	[-9.26; 9.66]	23.6%
Kaysen (3x) (2012)	42 83.30 25.00	42 83.50 24.10		-0.20	[-10.70; 10.30]	19.2%
Kaysen (6x) (2012)	45 87.80 28.60	45 88.60 28.20		-0.80	[-12.54; 10.94]	15.4%
Ipema (2012)	15 83.60 17.10	15 83.40 16.80		0.20	[-11.93; 12.33]	14.4%
Sikkes (2009)	14 74.24 17.57	14 71.83 16.56		2.41	[-10.24; 15.06]	13.2%
David (2009)	13 71.20 20.50	13 70.90 20.20		0.30	[-15.34; 15.94]	8.6%
Cravedi (2009)	7 61.80 14.50	7 61.40 21.80		0.40	[-19.00; 19.80]	5.6%
Random effects model	162	162		0.28	[-4.32; 4.88]	100%

Heterogeneity: I-squared=0%, tau-squared=0, p=0.9999

-10   0   10

5b

Studies on DBW	8-12 Months NHD Total Mean SD	Baseline Total Mean SD	Mean difference	MD	95%-CI	W(random)
Kaysen (2012)	42 84.10 25.6	42 83.50 24.10		0.60	[-10.03; 11.23]	25.1%
Kaysen (2012)	45 89.10 28.6	45 88.60 28.20		0.50	[-11.24; 12.24]	20.6%
Ipema (2012)	15 84.80 17.8	15 83.40 16.80		1.40	[-10.99; 13.79]	18.5%
Sikkes (2009)	14 76.76 18.5	14 71.83 16.56		4.93	[-8.08; 17.94]	16.8%
David (2009)	13 72.10 19.8	13 70.90 20.20		1.20	[-14.18; 16.58]	12.0%
Cravedi (2009)	7 63.40 15.8	7 61.40 21.80		2.00	[-17.94; 21.94]	7.1%
Random effects model	136	136		1.62	[-3.70; 6.95]	100%

Heterogeneity: I-squared=0%, tau-squared=0, p=0.9972

-20   -10   0   10   20

Fig 5. Dry body weight. (5a) Forest plot comparing dry body weight (DBW) in NHD patients at baseline (prior to beginning NHD) and after 4–6 months on NHD. (5b) Forest plot comparing dry body weight (DBW) in NHD patients at baseline (prior to beginning NHD) and after 8–12 months on NHD.

doi:10.1371/journal.pone.0157621.g005

in the percentage of body fat during one year of NHD [42]. The third study ascertained no change in fat mass during 12 months on NHD compared with a control group [17]. The use of a different measurement of fat mass precluded a meta-analysis.

Two studies reported the upper arm muscle area whereby one showed no change in MUAMC from baseline to 8 months NHD [39]. The other study showed no change in arm muscle area from baseline to 18 months NHD [42].

Three studies reported phase angle and had divergent outcomes [17,37,38]. As illustrated in Fig 7, phase angle did not significantly change from baseline to 12 months (mean difference 0.29°, 95% CI -0.004; 0.584, P = 0.05), although there was a positive trend. Influence analysis and funnel plot indicated no bias (data not shown).

Food records

Protein intake was measured in six studies, of which three could be used for the meta-analysis [14,39,40]. As shown in Fig 8, protein intake increased significantly from baseline to 4–6 months NHD (mean difference 18.9 g, 95% CI 9.7; 28.2, P<0.001). Influence analysis and funnel plot indicated no bias (data not shown).

Six studies reported energy intake, of which three could be used for meta-analysis [14,39,40]. As depicted in Fig 9, energy intake increased significantly between baseline and 4–6 months NHD (mean difference 183.2 kcal, 95% CI 16.8; 349.7, P = 0.03). The influence analysis
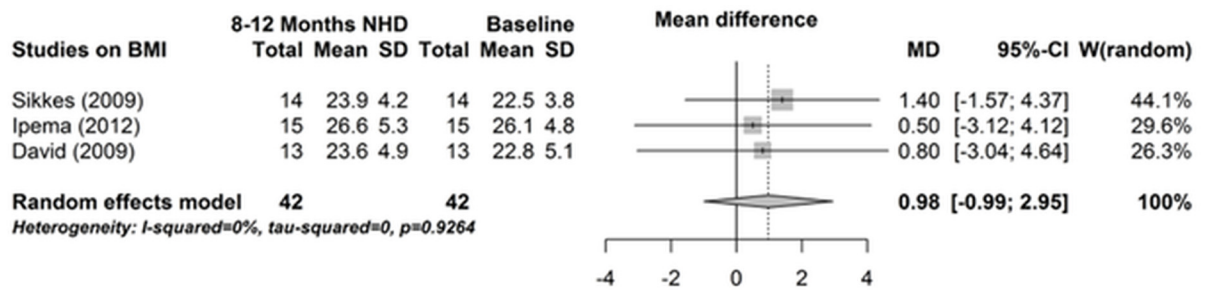
6a
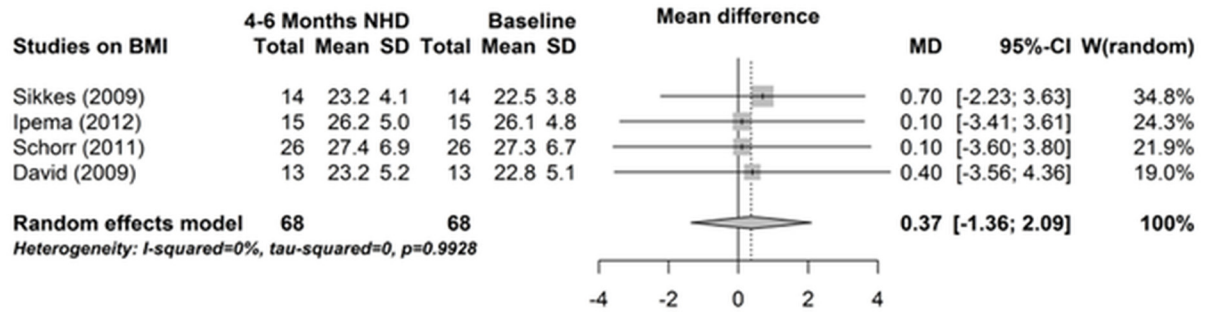
6b

Fig 6. Body mass index. (6a) Forest plot comparing body mass index (BMI) in NHD patients at baseline (prior to beginning NHD) and after 4–6 months on NHD. (6b) Forest plot comparing body mass index (BMI) in NHD patients at baseline (prior to beginning NHD) and after 8–12 months on NHD.
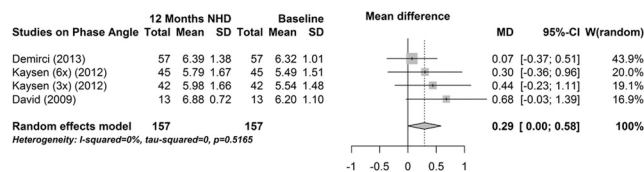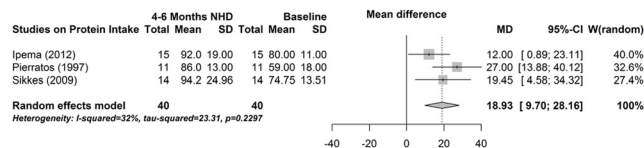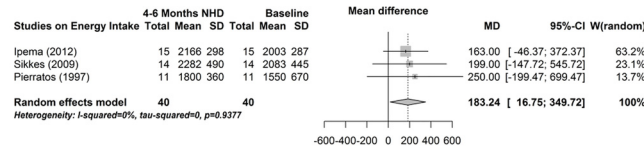
doi:10.1371/journal.pone.0157621.g006

Fig 7. Forest plot comparing phase angle in NHD patients at baseline (prior to beginning NHD) and after 12 months on NHD.

doi:10.1371/journal.pone.0157621.g007

Fig 8. Forest plot comparing protein intake in NHD patients at baseline (prior to beginning NHD) and after 4–6 months on NHD.

doi:10.1371/journal.pone.0157621.g008

Fig 9. Forest plot comparing energy intake in NHD patients at baseline (prior to beginning NHD) and after 4–6 months on NHD.

showed a change in the results after omitting one particular study ([Table 5](#)). The funnel plot indicated no bias (data not shown). There is a meta-effect, however, the degree of evidence is not very convincing.

Three studies measured carbohydrate intake and fat intake [14,39,41]. Meta analysis was not performed since only two of these studies were suitable [14,39]. None of the studies reported a significant change between baseline and 4 to12 months following the initiation of NHD [14,39,41].

Discussion

In our meta-analyses, we ascertained that NHD is associated with significantly higher protein intake, nPCR, and serum albumin compared with CHD. The results for serum albumin are strengthened by the meta-analysis of studies that prospectively compared patients receiving NHD and those who remained on CHD, which showed similar positive effects. Energy intake also increased but with moderate evidence. In contrast, the body composition parameters of dry body weight, BMI, and phase angle did not change after the initiation of NHD.

There is no 'gold standard' for the assessment of nutritional status in hemodialysis patients. In clinical practice, a combination of parameters is utilized such as the Subjective Global Assessment, anthropometry (dry body weight, body composition), nPCR, and serum albumin [43]. This meta-analysis shows that serum albumin levels increased significantly following the transition from CHD to NHD. Serum albumin is a measure of visceral protein stores and has prognostic significance in hemodialysis patients [44,45]. Although the increase in serum albumin during NHD may reflect genuine improvement in nutritional status, non-nutritional factors may contribute to the rise in serum albumin, e.g., improvement of systemic inflammation and/or reduction of proteinuria as a result of loss of residual renal function. It is unknown whether the increase in serum albumin after the transition to NHD translates into lower mortality. Notably, serum albumin is also a negative acute phase protein. However, CRP values did not significantly change post initiation of NHD [36–38]. This suggests that the increase in serum albumin levels during NHD is related to higher protein intake. This is substantiated by our meta-analyses demonstrating that both protein intake and nPCR increased significant after the transition from CHD to NHD. These effects were still evident after 8–12 months of receiving NHD. In accordance with these findings is the positive meta-effect for energy intake. These

Table 5. Influence analysis of energy intake between baseline and after 4–6 months of NHD.

	Mean difference	95% confidence interval	P-value
Omitting Ipema (2012)	218	-56.5–492.6	0.120
Omitting Pierratos (1997)	173	-6.6–351.8	0.059
Omitting Sikkes (2009)	179	-11.3–368.3	0.065
Pooled estimate	183	16.8–349.7	0.031

findings strongly posit that patients consume more nutrition following the transition to NHD. Sikkes et al indeed ascertained that 50% of NHD patients had an increased appetite after one year on NHD and that appetite appeared to improve more in patients with a lower baseline nPCR [14].

Previous studies showed better survival rates in HD patients with increasing weight and BMI [46,47] whereas weight loss is most commonly associated with a deterioration of nutritional status [43]. In our meta-analysis, dry body weight and BMI did not significantly vary during NHD. However, a change in body weight is not a sensitive parameter of nutritional status since it is affected by changes in lean body mass and hydration status. Various authors suggested that more frequent and/or longer hemodialysis sessions are associated with better control of extracellular volume leading to lower blood pressure with less antihypertensive medication [12,48–50]. Therefore, increases in lean body mass during NHD may be disregarded as a result of a contemporary reduction in extracellular fluid. Only three studies measured changes in fluid status during NHD [17,37,38]. Demirci et al indeed reported a significant decrease in ECW normalized for height and in ECW normalized for weight while both parameters increased in the control group of CHD patients [37]. David et al also reported a significant decrease in ECM/BCM from baseline to 6 months while receiving NHD [38]. In contrast, body water parameters, including ECW, did not alter during NHD in the study of Kaysen et al [17]. The minimal number of studies and the divergent results preclude a firm conclusion with regard to a possible substitution of extracellular fluid by lean body mass during NHD.

Lean body mass was measured with BIA in two studies and yielded different outcomes [17,37]. Kaysen et al determined no differences in lean body mass between the three times per week NHD group and the six times per week NHD group, although an insignificant decreasing trend after four months was indicated [17]. The study of Demirci et al showed significant increases in lean body mass and in fat mass in the NHD patients compared with the CHD controls in the course of one year [37]. Bioimpedance phase angle is a novel technique that may be exploited as a predictor for impaired muscle function and as an indicator for nutritional status, health related quality of life, forthcoming hospitalizations, and mortality [51]. Phase angle was measured in three studies and an insignificant positive trend in NHD patients was found in the meta-analysis.

In two studies, the upper arm muscle area was measured [39,42]. Spanner et al. discovered a steady decline in arm muscle area throughout the study period in NHD patients that could be due to accompanying loss in body weight that was also evident [42]. No change in muscle arm circumference in NHD patients was found in a study by Ipema et al [39]. The upper arm muscle area can be used for an estimation of the lean body mass and can be a predictor of mortality in hemodialysis patients [52,53]. On the other hand, it is not a very sensitive measurement being limited in reproducibility and has a relatively large inter-observer variability [53]. Overall, it can be concluded that our analysis does not provide evidence that body composition changes during NHD.

Remarkably, patients receiving NHD had a significantly higher protein and energy intake but did not exhibit an increase in BMI or dry body weight. This counter-intuitive finding may be explained by a negative protein balance induced by the NHD treatment. Various studies showed that hemodialysis while fasting is associated with a negative protein balance [54–56]. During NHD, patients are asleep and generally do not eat. It is feasible that the significant increase in protein intake in NHD patients is offset by increased losses of amino acids and increased hemodialysis-associated catabolism. Alternatively, the failure of patients to increase physical activity in order to increase fat free mass may play a role in the negative protein balance. None of the included studies measured daily activity and exercise in NHD patients. Chan et al studied exercise duration and capacity in patients after conversion to NHD and found an

improvement [57]. However, in a more recent study, it was found that NHD had no effect on physical performance, health, and functioning in the NHD group compared with the CHD group [58].

Although our systematic review and meta-analysis provides new information on the potential benefits of NHD, the results must be interpreted within the context of methodological limitations. First, most studies were constrained by a minimal sample size, the withdrawal of patients (on NHD) is not always described, a number of studies had incomplete dietary records for the participants, and, in several studies, the follow-up duration is relatively brief. Another limitation is the assumption that the experimental and control groups are independent. In cases with repeated measurement in the same group of subjects, such an assumption is not valid. However, meta-analysis programs do not account for the possibility of repeated measurements because these are rarely reported in complete detail. In these cases, however, our approach based on independence can be expected to underestimate the actual meta-effect. Considering the fact that there were only thirteen studies considered eligible for this review, we have decided not to exclude due to study design. This resulted in an extensively varied study design. Formal blinding of participants is impossible. To anticipate the limitations, several quality measurements were assessed. In all meta-analysis, we assessed homogeneity of effects, performed an influence analysis, and tested for funnel plot asymmetry. With a few exceptions, these tests did not provide evidence for bias. Notably, five out of the 14 meta-analyses were performed with only three studies. In three of these five meta-analyses a deviating influence analysis was found. Two of these were the meta-analyses of 'control group controlled' studies comparing albumin levels at 4–6 and at 12 months on NHD, respectively. The outcomes of these meta-analysis were used to corroborate the results of 'baseline controlled studies' comparing baseline with 4–6 and 8–12 months on NHD, respectively. The third meta-analysis with deviating influence analysis was on energy intake. Although, the three studies in this meta-analysis showed a uniform pattern, the deviating influence analysis precludes a definite conclusion on the effect of NHD on energy intake. There are no reviews published in regard to nutritional status in nocturnal hemodialysis patients to compare our results with or to be able to reconsider any type of disagreements in outcomes.

Conclusions and Recommendations

This systematic review illustrates that NHD is associated with a significantly higher protein- and energy intake and increases in serum albumin and nPCR. Prospective randomized trials should be conducted to add more evidence to the effect of the transition from CHD to NHD on nutritional status in its various facets: food intake, laboratory parameters, and body composition. Additionally, future studies should address the important question whether the higher protein intake during NHD translates into a lower morbidity and mortality. Finally, more research should be devoted to the effect of combined treatment with intensive NHD and an exercise program on body composition.

Supporting Information

S1 Fig. Albumin (Kaysen 3x per week NHD instead of 6x per week NHD [17]). (A) Forrest plot comparing albumin in NHD patients on baseline (before transition from CHD to NHD) and control CHD patients. **(B)** Forrest plot comparing albumin in NHD patients after 4–6 months on NHD and control CHD patients after 4–6 months follow up. **(C)** Forrest plot comparing albumin in NHD patients after 12 months on NHD and control CHD patients after 12 months follow up.
(PDF)

S1 File. Protocol systematic review.
(PDF)

S1 Table. PRISMA 2009 checklist. Checklist of this systematic review and meta-analyses.
(PDF)

S2 Table. Summary of the results of the 13 studies. Summary of the results of the 13 studies
on the nutritional status of nocturnal hemodialysis patients.
(PDF)

Author Contributions

Conceived and designed the experiments: KJRI SS AV RW CFMF. Performed the experiments: KJRI SS AV RW CFMF. Analyzed the data: KJRI SS AV WPK CFMF. Contributed reagents/materials/analysis tools: KJRI RW CPS CAJMG CFMF. Wrote the paper: KJRI SS AV RW CPS CAJMG WPK CFMF.

References

1. Araujo IC, Kamimura MA, Draibe SA, Canziani ME, Manfredi SR, Avesani CM, et al. Nutritional parameters and mortality in incident hemodialysis patients. J Ren Nutr. 2006; 16: 27–35. PMID: 16414438

2. Herselman M, Moosa MR, Kotze TJ, Kritzinger M, Wuister S, Mostert D. Protein-energy malnutrition as a risk factor for increased morbidity in long-term hemodialysis patients. J Ren Nutr. 2000; 10: 7–15. PMID: 10671628

3. Lindholm B, Wang T, Heimburger O, Bergstrom J. Influence of different treatments and schedules on the factors conditioning the nutritional status in dialysis patients. Nephrol Dial Transplant. 1998; 13 Suppl 6: 66–73. PMID: 9719208

4. Bossola M, Muscaritoli M, Tazza L, Panocchia N, Liberatori M, Giungi S, et al. Variables associated with reduced dietary intake in hemodialysis patients. J Ren Nutr. 2005; 15: 244–252. PMID: 15827898

5. Burrowes JD, Larive B, Chertow GM, Cockram DB, Dwyer JT, Greene T, et al. Self-reported appetite, hospitalization and death in haemodialysis patients: Findings from the hemodialysis (HEMO) study. Nephrol Dial Transplant. 2005; 20: 2765–2774. PMID: 16204298

6. Johansen KL, Shubert T, Doyle J, Soher B, Sakkas GK, Kent-Braun JA. Muscle atrophy in patients receiving hemodialysis: Effects on muscle strength, muscle quality, and physical function. Kidney Int. 2003; 63: 291–297. PMID: 12472795

7. Qureshi AR, Alvestrand A, Divino-Filho JC, Gutierrez A, Heimburger O, Lindholm B, et al. Inflammation, malnutrition, and cardiac disease as predictors of mortality in hemodialysis patients. J Am Soc Nephrol. 2002; 13 Suppl 1: S28–36. PMID: 11792759

8. Johansen KL, Kaysen GA, Young BS, Hung AM, da Silva M, Chertow GM. Longitudinal study of nutritional status, body composition, and physical function in hemodialysis patients. Am J Clin Nutr. 2003; 77: 842–846. PMID: 12663281

9. McFarlane PA. Nocturnal hemodialysis: Effects on solute clearance, quality of life, and patient survival. Curr Opin Nephrol Hypertens. 2011; 20: 182–188. doi: 10.1097/MNH.0b013e3283437046 PMID: 21252663

10. Lacson E Jr., Wang W, Lester K, Ofsthun N, Lazarus JM, Hakim RM. Outcomes associated with in-center nocturnal hemodialysis from a large multicenter program. Clin J Am Soc Nephrol. 2010; 5: 220–226. doi: 10.2215/CJN.06070809 PMID: 19965529

11. Walsh M, Culleton B, Tonelli M, Manns B. A systematic review of the effect of nocturnal hemodialysis on blood pressure, left ventricular hypertrophy, anemia, mineral metabolism, and health-related quality of life. Kidney Int. 2005; 67: 1500–1508. PMID: 15780103

12. Charra B, Calemard E, Ruffet M, Chazot C, Terrat JC, Vanel T, et al. Survival as an index of adequacy of dialysis. Kidney Int. 1992; 41: 1286–1291. PMID: 1614043

13. Pierratos A. The case for nocturnal hemodialysis. ASAIO J. 2001; 47: 446–448. PMID: 11575811

14. Sikkes ME, Kooistra MP, Weijs PJ. Improved nutrition after conversion to nocturnal home hemodialysis. J Ren Nutr. 2009; 19: 494–499. doi: 10.1053/j.jrn.2009.05.006 PMID: 19616453

15. Wells GA, Shea B, O'Connel D, Peterson J, Welch V, Losos M, et al. The newcastle-ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

16. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to meta-analysis. West Sussex, United Kingdom: John Wiley & Sons, Ltd; 2009.

17. Kaysen GA, Greene T, Larive B, Mehta RL, Lindsay RM, Depner TA, et al. The effect of frequent hemodialysis on nutrition and body composition: Frequent hemodialysis network trial. Kidney Int. 2012; 82: 90–99. doi: 10.1038/ki.2012.75 PMID: 22456602

18. Cravedi P, Ruggenenti P, Mingardi G, Sghirlanzoni MC, Remuzzi G. Thrice-weekly in-center nocturnal hemodialysis: An effective strategy to optimize chronic dialysis therapy. Int J Artif Organs. 2009; 32: 12–19. PMID: 19241359

19. Clajus C, Kielstein JT, Haller H, David S. Prospective longitudinal evaluation of in-center conversion from conventional to intensified nocturnal hemodialysis. Nephrol Dial Transplant. 2012; 27: ii220.

20. McPhatter L, L. Dietary management of the nocturnal home hemodialysis patient. Nephrol News Issues. 2012; 26: 29.

21. Fourie E, Stevens S, Becker C. In-centre nocturnal haemodialysis optimising chronic dialysis therapy—first experiences in south africa. Cardiovas J Afri. 2010; 21: S10.

22. Martins AR, Parreira L, Duque AS, Rodrigues I. Extended nocturnal hemodialysis: Single center experience. Nephrol Dial Transplant. 2013; 28: i205.

23. Moran J, Silva-Brown R, Bond TC, Provenzano R. Biochemical nutritional parameters of a large US in-center nocturnal hemodialysis population. Hemodial Int. 2012; 16: 164.

24. Von Gersdorff G, Weinreich T, Duttlinger J, Schaller M, Barth C. Nocturnal hemodialysis in germany: A case control study. NDT Plus. 2010; 3: iii142.

25. Lacson E Jr, Diaz-Buxo JA. Daily and nocturnal hemodialysis: How do they stack up? Am J Kidney Dis. 2001; 38: 225–239. PMID: 11479147

26. Gubensek J, Buturovic-Ponikvar J, Knap B, Marn Pernat A, Benedik M, Ponikvar R. Effect of switching to nocturnal thrice-weekly hemodialysis on clinical and laboratory parameters: Our experience. Ther Apheresis Dial. 2013; 17: 412–415.

27. Lindsay RM. The london, ontario, daily/nocturnal hemodialysis study. Sem Dialysis. 2004; 17: 85–91.

28. Mahadevan K, Pellicano R, Reid A, Kerr P, Polkinghorne K, Agar J. Comparison of biochemical, haematological and volume parameters in two treatment schedules of nocturnal home haemodialysis. Nephrology. 2006; 11: 413–418. PMID: 17014555

29. Ouwendyk M, Pierratos A, Francoeur R, Wallace L, Sit W, Vas S. Slow nocturnal home hemodialysis (SNHHD)—one year later. J CANNT. 1996; 6: 26–28.

30. Lacson E Jr., Xu J, Suri RS, Nesrallah G, Lindsay R, Garg AX, et al. Survival with three-times weekly in-center nocturnal versus conventional hemodialysis. J Am Soc Nephrol. 2012; 23: 687–695. doi: 10.1681/ASN.2011070674 PMID: 22362905

31. Suri R, Depner TA, Blake PG, Heidenheim AP, Lindsay RM. Adequacy of quotidian hemodialysis. Am J Kidney Dis. 2003; 42: 42–48. PMID: 12830443

32. Rocco MV, Lockridge RS Jr., Beck GJ, Eggers PW, Gassman JJ, Greene T, et al. The effects of frequent nocturnal home hemodialysis: The frequent hemodialysis network nocturnal trial. Kidney Int. 2011; 80: 1080–1091. doi: 10.1038/ki.2011.213 PMID: 21775973

33. O'Sullivan DA, McCarthy JT, Kumar R, Williams AW. Improved biochemical variables, nutrient intake, and hormonal factors in slow nocturnal hemodialysis: A pilot study. Mayo Clin Proc. 1998; 73: 1035–1045. PMID: 9818036

34. McPhatter LL, Lockridge RS Jr, Albert J, Anderson H, Craft V, Jennings FM, et al. Nightly home hemodialysis: Improvement in nutrition and quality of life. Adv Ren Replace Ther. 1999; 6: 358–365. PMID: 10543717

35. Alloatti S, Molino A, Manes M, Bonfant G, Pellu V. Long nocturnal dialysis. Blood Purif. 2002; 20: 525–530. PMID: 12566667

36. Maduell F, Arias M, Duran CE, Vera M, Fontsere N, Azqueta M, et al. Nocturnal, every-other-day, online haemodiafiltration: An effective therapeutic alternative. Nephrol Dial Transplant. 2012; 27: 1619–1631. doi: 10.1093/ndt/gfr491 PMID: 21931125

37. Demirci C, Ozkahya M, Demirci MS, Asci G, Kose T, Colak T, et al. Effects of three times weekly eight-hour nocturnal hemodialysis on volume and nutritional status. Am J Nephrol. 2013; 37: 559–567. doi: 10.1159/000351182 PMID: 23735837

38. David S, Kumpers P, Eisenbach GM, Haller H, Kielstein JT. Prospective evaluation of an in-centre conversion from conventional haemodialysis to an intensified nocturnal strategy. Nephrol Dial Transplant. 2009; 24: 2232–2240. doi: 10.1093/ndt/gfp029 PMID: 19208770

39. Ipema KJ, van der Schans CP, Vonk N, de Vries JM, Westerhuis R, Duym E, et al. A difference between day and night: Protein intake improves after the transition from conventional to frequent nocturnal home hemodialysis. J Ren Nutr. 2012; 22: 365–372. doi: 10.1053/j.jrn.2011.08.010 PMID: 22054873

40. Pierratos A, Ouwendyk M, Francoeur R, Vas S, Raj DS, Ecclestone AM, et al. Nocturnal hemodialysis: Three-year experience. J Am Soc Nephrol. 1998; 9: 859–868. PMID: 9596084

41. Schorr M, Manns BJ, Culleton B, Walsh M, Klarenbach S, Tonelli M, et al. The effect of nocturnal and conventional hemodialysis on markers of nutritional status: Results from a randomized trial. J Renal Nutr. 2011; 21: 271–276.

42. Spanner E, Suri R, Heidenheim AP, Lindsay RM. The impact of quotidian hemodialysis on nutrition. Am J Kidney Dis. 2003; 42: 30–35. PMID: 12830441

43. Fouque D, Vennegoor M, ter Wee P, Wanner C, Basci A, Canaud B, et al. EBPG guideline on nutrition. Nephrol Dial Transplant. 2007; 22 Suppl 2: ii45–87. PMID: 17507426

44. Ikizler TA, Wingard RL, Harvell J, Shyr Y, Hakim RM. Association of morbidity with markers of nutrition and inflammation in chronic hemodialysis patients: A prospective study. Kidney Int. 1999; 55: 1945–1951. PMID: 10231458

45. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE. Hypoalbuminemia, cardiac morbidity, and mortality in end-stage renal disease. J Am Soc Nephrol. 1996; 7: 728–736. PMID: 8738808

46. Abbott KC, Glanton CW, Trespalacios FC, Oliver DK, Ortiz MI, Agodoa LY, et al. Body mass index, dialysis modality, and survival: Analysis of the united states renal data system dialysis morbidity and mortality wave II study. Kidney Int. 2004; 65: 597–605. PMID: 14717930

47. Leavey SF, McCullough K, Hecking E, Goodkin D, Port FK, Young EW. Body mass index and mortality in 'healthier' as compared with 'sicker' haemodialysis patients: Results from the dialysis outcomes and practice patterns study (DOPPS). Nephrol Dial Transplant. 2001; 16: 2386–2394. PMID: 11733631

48. Kooistra MP, Vos J, Koomans HA, Vos PF. Daily home haemodialysis in the netherlands: Effects on metabolic control, haemodynamics, and quality of life. Nephrol Dial Transplant. 1998; 13: 2853–2860. PMID: 9829490

49. Charra B, Laurent G, Chazot C, Calemard E, Terrat JC, Vanel T, et al. Clinical assessment of dry weight. Nephrol Dial Transplant. 1996; 11 Suppl 2: 16–19. PMID: 8803988

50. Charra B. Fluid balance, dry weight, and blood pressure in dialysis. Hemodial Int. 2007; 11: 21–31. PMID: 17257351

51. Beberashvili I, Azar A, Sinuani I, Shapiro G, Feldman L, Stav K, et al. Bioimpedance phase angle predicts muscle function, quality of life and clinical outcome in maintenance hemodialysis patients. Eur J Clin Nutr. 2014; 68: 683–689. doi: 10.1038/ejcn.2014.67 PMID: 24736681

52. Stosovic M, Stanojevic M, Simic-Ogrizovic S, Jovanovic D, Djukanovic L. The predictive value of anthropometric parameters on mortality in haemodialysis patients. Nephrol Dial Transplant. 2011; 26: 1367–1374. doi: 10.1093/ndt/gfq497 PMID: 20713977

53. Noori N, Kovesdy CP, Bross R, Lee M, Oreopoulos A, Benner D, et al. Novel equations to estimate lean body mass in maintenance hemodialysis patients. Am J Kidney Dis. 2011; 57: 130–139. doi: 10.1053/j.ajkd.2010.10.003 PMID: 21184920

54. Raj DS, Zager P, Shah VO, Dominic EA, Adeniyi O, Blandon P, et al. Protein turnover and amino acid transport kinetics in end-stage renal disease. Am J Physiol Endocrinol Metab. 2004; 286: E136–43. PMID: 13129859

55. Ikizler TA, Pupim LB, Brouillette JR, Levenhagen DK, Farmer K, Hakim RM, et al. Hemodialysis stimulates muscle and whole body protein loss and alters substrate oxidation. Am J Physiol Endocrinol Metab. 2002; 282: E107–16. PMID: 11739090

56. Veeneman JM, Kingma HA, Boer TS, Stellaard F, De Jong PE, Reijngoud DJ, et al. Protein intake during hemodialysis maintains a positive whole body protein balance in chronic hemodialysis patients. Am J Physiol Endocrinol Metab. 2003; 284: E954–65. PMID: 12540372

57. Chan CT, Notarius CF, Merlocco AC, Floras JS. Improvement in exercise duration and capacity after conversion to nocturnal home haemodialysis. Nephrol Dial Transplant. 2007; 22: 3285–3291. PMID: 17595181

58. Hall YN, Larive B, Painter P, Kaysen GA, Lindsay RM, Nissenson AR, et al. Effects of six versus three times per week hemodialysis on physical performance, health, and functioning: Frequent hemodialysis network (FHN) randomized trials. Clin J Am Soc Nephrol. 2012; 7: 782–794. doi: 10.2215/CJN.10601011 PMID: 22422538