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Biocompatible dialysis fluids for peritoneal dialysis (Review)

Htay H, Johnson DW, Wiggins KJ, Badve SV, Craig JC, Strippoli GFM, Cho Y

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Biocompatible dialysis fluids for peritoneal dialysis (Review)

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[Intervention Review]

Biocompatible dialysis fluids for peritoneal dialysis

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ABSTRACT

Background

Biocompatible peritoneal dialysis (PD) solutions, including neutral pH, low glucose degradation product (GDP) solutions and icodextrin, have previously been shown to favourably influence some patient-level outcomes, albeit based on generally sub-optimal quality studies. Several additional randomised controlled trials (RCT) evaluating biocompatible solutions in PD patients have been published recently. This is an update of a review first published in 2014.

Objectives

This review aimed to look at the benefits and harms of biocompatible PD solutions in comparison to standard PD solutions in patients receiving PD.

Search methods

The Cochrane Kidney and Transplant Specialised Register was searched up to 12 February 2018 through contact with the Information Specialist using search terms relevant to this review. Studies in the Specialised Register are identified through searches of CENTRAL, MEDLINE, and EMBASE, conference proceedings, the International Clinical Trials Register Search Portal and ClinicalTrials.gov.

Selection criteria

All RCTs and quasi-RCTs in adults and children comparing the effects of biocompatible PD solutions (neutral pH, lactate-buffered, low GDP; neutral pH, bicarbonate(± lactate)-buffered, low GDP; glucose polymer (icodextrin)) in PD were included. Studies of amino acid-based solutions were excluded.

Data collection and analysis

Two authors extracted data on study quality and outcomes. Summary effect estimates were obtained using a random-effects model, and results were expressed as risk ratios and 95% confidence intervals (CI) for categorical variables, and mean differences (MD) or standardised mean differences (SMD) and 95% CI for continuous variables.

Main results

This review update included 42 eligible studies (3262 participants), including six new studies (543 participants). Overall, 29 studies (1971 participants) compared neutral pH, low GDP PD solution with conventional PD solution, and 13 studies (1291 participants) compared icodextrin with conventional PD solution. Risk of bias was assessed as high for sequence generation in three studies, allocation concealment in three studies, attrition bias in 21 studies, and selective outcome reporting bias in 16 studies.

Neutral pH, low GDP versus conventional glucose PD solution

Use of neutral pH, low GDP PD solutions improved residual renal function (RRF) preservation (15 studies, 835 participants: SMD 0.19, 95% CI 0.05 to 0.33; high certainty evidence). This approximated to a mean difference in glomerular filtration rate of 0.54 mL/min/1.73 m² (95% CI 0.14 to 0.93). Better preservation of RRF was evident at all follow-up durations with progressively greater preservation observed with increasing follow up duration. Neutral pH, low GDP PD solution use also improved residual urine volume preservation (11 studies, 791 participants: MD 114.37 mL/day, 95% CI 47.09 to 181.65; high certainty evidence). In low certainty evidence, neutral pH, low GDP solutions may make little or no difference to 4-hour peritoneal ultrafiltration (9 studies, 414 participants: SMD -0.42, 95% CI -0.74 to -0.10) which approximated to a mean difference in peritoneal ultrafiltration of 69.72 mL (16.60 to 122.00 mL) lower, and may increase dialysate:plasma creatinine ratio (10 studies, 746 participants: MD 0.01, 95% CI 0.00 to 0.03), technique failure or death compared with conventional PD solutions. It is uncertain whether neutral pH, low GDP PD solution use led to any differences in peritonitis occurrence, hospitalisation, adverse events (6 studies, 519 participants) or inflow pain (1 study, 58 participants: RR 0.51, 95% CI 0.24 to 1.08).

Glucose polymer (icodextrin) versus conventional glucose PD solution

In moderate certainty evidence, icodextrin probably reduced episodes of uncontrolled fluid overload (2 studies, 100 participants: RR 0.30, 95% CI 0.15 to 0.59) and augmented peritoneal ultrafiltration (4 studies, 102 participants: MD 448.54 mL/d, 95% CI 289.28 to 607.80) without compromising RRF (4 studies, 114 participants: SMD 0.12, 95% CI -0.26 to 0.49; low certainty evidence) which approximated to a mean creatinine clearance of 0.30 mL/min/1.73m² higher (0.65 lower to 1.23 higher) or urine output (3 studies, 69 participants: MD -88.88 mL/d, 95% CI -356.88 to 179.12; low certainty evidence). It is uncertain whether icodextrin use led to any differences in adverse events (5 studies, 816 participants) technique failure or death.

Authors' conclusions

This updated review strengthens evidence that neutral pH, low GDP PD solution improves RRF and urine volume preservation with high certainty. These effects may be related to increased peritoneal solute transport and reduced peritoneal ultrafiltration, although the evidence for these outcomes is of low certainty due to significant heterogeneity and suboptimal methodological quality. Icodextrin prescription increased peritoneal ultrafiltration and mitigated uncontrolled fluid overload with moderate certainty. The effects of either neutral pH, low GDP solution or icodextrin on peritonitis, technique survival and patient survival remain uncertain and require further high quality, adequately powered RCTs.

PLAIN LANGUAGE SUMMARY

Biocompatible dialysis fluids for peritoneal dialysis

What is the issue?

Peritoneal dialysis is a form of dialysis therapy for people with kidney failure delivered at home. Patients are required to use peritoneal dialysis solutions to perform the dialysis by putting solution in their abdomen. Peritoneal dialysis uses the lining of the abdomen called the "peritoneal membrane" as a filter, across which toxins and fluids are removed from the body. The longevity of peritoneal dialysis can be limited by peritoneal membrane injury, which is partly as a result of biologically 'unfriendly' peritoneal dialysis solutions, which are acidic and consist of high levels of glucose and toxic glucose breakdown products. To overcome these hurdles, biocompatible peritoneal dialysis solutions (i.e. with a neutral pH and low levels of glucose breakdown products or with a glucose-alternative like icodextrin) have been manufactured with the aim of providing patient benefit.

What did we do?

We conducted a review of the literature to examine the benefits and harms from the use of biocompatible peritoneal dialysis solutions.

What did we find?

We identified 42 studies (3262 participants) examining the effects of these solutions on patient outcomes. When compared to conventional peritoneal dialysis solutions, we found that neutral pH, low glucose breakdown product peritoneal dialysis solutions resulted in better preservation of a patient's own kidney function including urine output. Patients who received non-glucose based (icodextrin) peritoneal dialysis solutions achieved greater fluid removal with their dialysis and were 70% less likely to experience uncontrolled episodes of fluid overload. No significant harms were identified with any of the biocompatible peritoneal dialysis solutions. Many of the studies were limited by small size, short follow-up duration, suboptimal methodological quality, and inconsistent reporting of outcomes. Consequently, the

effects of biocompatible peritoneal dialysis solutions on the length of time that a patient is able to either remain on peritoneal dialysis or stay alive are uncertain.

Conclusions

Compared with peritoneal dialysis patients treated with conventional peritoneal dialysis solutions, those treated with biocompatible solutions experience important benefits including better preservation of their own kidney function and urine volume with neutral pH, low glucose breakdown product peritoneal dialysis solutions and more effective prevention of fluid overload due to increased dialysis-related fluid removal with icodextrin. Whether these benefits help patients to stay on peritoneal dialysis longer or live longer are uncertain and require further study.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Low GDP (all buffer types) compared to standard glucose dialysate for peritoneal dialysis (PD)

Neutral pH, low GDP PD solutions versus standard glucose PD solutions

Patient or population: PD patients

Setting: community

Intervention: neutral, low GDP dialysate (all buffer types)

Comparison: standard glucose dialysate

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard glucose dialysate	Risk with low GDP dialysate (all buffer types)				
Residual renal function (GFR; follow-up 3 months to more than 3 years)	The mean residual renal function (GFR) was 0.54 mL/min/1.73 m ² higher with low GDP dialysate (0.14 to 0.93 higher) compared to standard glucose dialysate		-	835 (15)	⊕⊕⊕⊕ HIGH ^a	SMD 0.19 higher (0.05 to 0.33 higher)
Urine volume (follow-up to more than 3 years)	The mean urine volume was 114.37 mL/d higher with low GDP dialysate (47.09 to 181.65 higher) compared to standard glucose dialysate		-	791 (11)	⊕⊕⊕⊕ HIGH ^b	-
Peritoneal ultrafiltration: 4 hours (follow-up to 24 months)	The estimated mean peritoneal ultrafiltration 69.72 mL/4 hours lower with low GDP dialysate (16.60 to 122.84 lower) compared to standard glucose dialysate		-	414 (9)	⊕⊕⊕⊖ LOW ¹	-
Peritoneal solute transport rate (4-hour dialysis:plasma creatinine) (follow-up to more than 3 years)	The mean peritoneal solute transport rate was 0.01 higher with low GDP dialysate (0 to 0.03 higher) compared to standard glucose dialysate		-	746 (10)	⊕⊕⊕⊖ LOW ²	SMD 0.42 lower (0.74 to 0.10 lower)
Peritonitis rate (episodes/total patient-months) (up to 24 months)	31 per 1,000	36 per 1,000 (26 to 51)	RR 1.18 (0.84 to 1.64)	18,184 (10)	⊕⊕⊕⊖ LOW ³	-
Technique failure (death-censored)	74 per 1,000	81 per 1,000 (55 to 120)	RR 1.10 (0.75 to 1.63)	1275 (15)	⊕⊕⊕⊖ LOW ⁴	-

(follow-up to more than 3 years)						
Death (all causes) (follow-up to more than 3 years)	77 per 1,000	21 fewer per 1,000 (41 fewer to 11 more)	RR 0.73 (0.47 to 1.14)	1229 (15)	⊕⊕⊕⊕ LOW ⁴	-

In very low certainty evidence, it is uncertain whether neutral pH, low GDP solution use led to any differences in inflow pain compared with standard PD solution (1 studies, 58 participants)

In very low certainty evidence, it is uncertain whether neutral pH, low GDP solution use led to adverse events including exit site/tunnel infection, non-PD related infection/general infection, inadequate dialysis, fluid overload/hypervolaemia, hypertension, hypotension, hernia, peritoneal leak, catheter blockage, malposition, gastrointestinal disorder, abdominal pain, pancreatitis, enteritis, vomiting, newly diagnosed cancer, arthritis, angina, apoplexy, hypercalcaemia, hypocalcaemia, hyperphosphataemia, and hyperglycaemia (6 studies, 519 participants).

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GFR: glomerular filtration rate

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

^a Benefit was evident at all time points assessed

^b Benefit was greater with longer follow-up duration (i.e. longer than 12 months)

¹ Downgraded two levels for moderate level of heterogeneity which could not be explained and indirectness

² Downgraded two levels for very serious study limitation significantly different baseline peritoneal solute transport rate in 30% of studies

³ Downgraded two levels for study limitation (high risk of attrition bias amongst studies analysed) and moderate heterogeneity observed

⁴ Downgraded two levels for very serious study limitation (none of the studies were adequately powered and number after combining studies remained too small to accurately assess this outcome)

Summary of findings 2. Glucose polymer (icodextrin) compared to standard glucose dialysate for peritoneal dialysis (PD)

Glucose polymer (icodextrin) compared to standard glucose dialysate for PD

Patient or population: PD patients

Setting: community

Intervention: glucose polymer (icodextrin)

Comparison: standard glucose dialysate

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard glucose dialysate	Risk with glucose polymer (icodextrin)				
Uncontrolled fluid overload (follow-up to 24 months)	531 per 1,000	159 per 1,000 (80 to 313)	RR 0.30 (0.15 to 0.59)	100 (2)	⊕⊕⊕⊖ MODERATE ¹	-
Rash (follow-up to 12 months)	43 per 1,000	109 per 1,000 (26 to 466)	RR 2.51 (0.59 to 10.72)	755 (3)	⊕⊕⊖⊖ LOW ²	-
Residual renal function (renal CrCl) (follow-up to 24 months)	The mean residual renal function (renal CrCl) was 0.30 mL/min higher with icodextrin (0.65 lower to 1.23 higher) than standard glucose dialysate		-	114 (4)	⊕⊕⊖⊖ LOW ³	SMD 0.12 higher (0.26 lower to 0.49 higher)
Urine volume (follow-up to 24 months)	The mean urine volume was 88.88 mL/d lower with icodextrin (356.88 lower to 179.12 higher) than standard glucose dialysate		-	69 (3)	⊕⊕⊖⊖ LOW ³	-
Daily ultrafiltration (follow-up to 24 months)	The mean daily ultrafiltration was 448.54 mL/d higher with icodextrin (289.28 to 607.8 higher) than standard glucose dialysate		-	102 (4)	⊕⊕⊕⊖ MODERATE ¹	-
Peritonitis (follow-up to 24 months)	236 per 1,000	12 fewer per 1,000 (54 fewer to 42 more)	RR 0.95 (0.77 to 1.18)	667 (6)	⊕⊕⊖⊖ LOW ⁴	-
Technique failure (death-censored) (up to 24 months)	107 per 1,000	64 per 1,000 (34 to 120)	RR 0.60 (0.32 to 1.12)	350 (4)	⊕⊖⊖⊖ VERY LOW ⁵	-

In very low certainty evidence, it is uncertain whether icodextrin use led to any difference in death (all causes) compared to standard glucose solution (6 studies, 816 participants).

In very low certainty evidence, it is uncertain whether icodextrin use led to any difference in adverse events including abdominal discomfort, anaemia, arterial emboli, cardiac failure, cerebrovascular accident, diabetic foot, dizzy, electrolyte disturbances, exit site infection, fatigue, fluid overload, headache, stroke, hyperglycaemia, hypotension, myocardial infarction, pain, pleural effusion, pneumonia, pulmonary embolism, thirsty, uncontrolled hypertension, congestion, upper respiratory tract infection, and vomiting (5 studies, 816 participants).

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

CrCl: creatinine clearance; **GFR:** glomerular filtration rate

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded one level for imprecision (small number of included studies and participants)

² Downgraded two levels for imprecision (small number of included studies and participants) and study limitation (high attrition bias)

³ Downgraded two levels for imprecision (small number of included studies and participants) and study limitation (limited number of long-term studies)

⁴ Downgraded two levels for very serious study limitation (high attrition bias, limited number of long-term studies)

⁵ Downgraded three levels for imprecision (small number of included studies and participants) and very serious study limitation (limited number of long-term studies, studies were not adequately powered to detect a difference in technique survival)

⁶ Studies were not adequately powered to detect a difference in technique survival

BACKGROUND

Description of the condition

Peritoneal dialysis (PD) is a widely utilised and highly cost-effective method of renal replacement therapy that is practised by approximately 11% of the world's population (Li 2017). Its annual global growth rate of 8% per annum exceeds that of haemodialysis (HD) (6% to 7% per annum) (Li 2017) and public policy changes in some parts of the world (e.g. Thailand and USA) have triggered unprecedented expansion of the therapy (Mehrotra 2016). Compared with HD, PD offers a number of advantages including better preservation of residual renal function (RRF), improved quality of life, greater treatment satisfaction, improved ability to provide incremental dialysis, deferred need for vascular access creation, reduced bacteraemia risk, reduced hepatitis transmission, less restricted diet and lifestyle, greater ability to travel, and possibly superior survival in the first few years after dialysis (Nadeau-Fredette 2015). Additional advantages in lower income countries include reduced requirements for technical support and electricity, treatment simplicity, lesser need for trained clinical staff and lower propensity to be adversely affected by natural disasters (Li 2017). Improvements in PD patient survival have outstripped those of HD patients and progressive technical innovations have allowed patients to remain on PD for longer periods of time (Li 2017). However, the majority of PD patients ultimately transfer to HD after a few years, primarily because of infection, membrane failure, mechanical complications or patient burnout (Lan 2016).

A significant factor underpinning PD technique failure is the development of structural and functional changes of the peritoneal membrane with increasing PD duration (Williams 2003). These changes include thickening of the submesothelial compact collagenous zone and subendothelial hyalinisation of post-capillary venules, with obliteration or narrowing of the vascular lumen (Williams 2003). The risk of encapsulating peritoneal sclerosis also increases with longer duration of PD (Brown 2009; Brown 2017; Johnson 2010; Rigby 1998). Progressive damage to the peritoneal membrane contributes to inadequate solute clearance, ultrafiltration (UF) failure, and change in peritoneal membrane transport properties, thereby affecting the ability of the membrane to function adequately. Loss of RRF also contributes to both UF failure and reduced solute clearance and is a predictor of increased death (Bargman 2001).

Both peritoneal membrane changes and loss of RRF in PD patients may be at least partly related to the use of PD solutions. Conventional PD solutions have an acidic pH and rely on hyperosmolar dextrose solutions to achieve an adequate gradient for UF across the peritoneal membrane (Szeto 2017). Their low pH and hyperosmolarity have been implicated in acute toxicity, such as inflow pain (Cho 2012; Nataatmadja 2017; Szeto 2017). Furthermore, heat sterilisation of PD solutions results in generation of glucose degradation products (GDP) (Nilsson-Thorell 1993; Wieslander 1996), which in turn leads to formation of advanced glycation end products (AGE) (Lamb 1995; Nakayama 1997) and possibly to chronic peritoneal membrane toxicity, such as increased peritoneal solute transport rate, membrane fibrosis and neovascularisation, membrane failure and encapsulating peritoneal sclerosis (Mateijsen 1999; Pollock 2005; Szeto 2017). Damage to the peritoneal membrane may also impair host defences and predispose patients to peritonitis (Jorres 1992;

Topley 1997). Finally, systemic absorption of GDPs may lead to direct nephrotoxicity and loss of RRF (Justo 2005).

Description of the intervention

Newer, biocompatible, dialysis solutions have been designed to minimise perturbation of the physiological milieu in the peritoneal cavity. The main approaches to creation of biocompatible solutions have been generation of solutions with a neutral pH and low GDP content, use of bicarbonate ($\pm$ lactate) buffer, substitution of dextrose with glucose polymers (resulting in low GDP content albeit with an acidic pH), and use of amino acids as the osmotic agent.

How the intervention might work

Results of in vitro studies and small studies using surrogate end points suggest that biocompatible PD fluids may cause less damage to the peritoneal membrane than conventional fluids, and hence may improve patient outcomes (Mortier 2004; Mortier 2005). Improvement in peritoneal morphology with use of biocompatible PD solution has also been reported (Ayuzawa 2012). Furthermore, use of glucose polymer PD solution has been shown to augment peritoneal UF (Johnson 2003). Reduced exposure to GDP in biocompatible PD solutions may also lead to reduced systemic GDP absorption and ensuing nephrotoxicity (Justo 2005).

Why it is important to do this review

In comparison to conventional PD solutions, biocompatible solutions are more costly in some countries and the effect of these solutions on 'hard' (patient-level clinical outcomes) endpoints are unclear. Furthermore, their role in clinical practice has not been established

OBJECTIVES

This review aimed to look at the benefits and harms of biocompatible PD solutions in comparison to standard PD solutions in patients receiving PD.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) looking at the effects of biocompatible dialysis solutions on patient outcomes in PD. The first period of randomised cross-over studies was also included. When it was not possible to establish which data from cross-over studies was from the first arm of the study, studies were excluded from the meta-analysis.

Types of participants

Adults and children receiving any type of home-based PD (continuous ambulatory PD (CAPD) or automated PD (APD)).

Types of interventions

Studies comparing the treatment of biocompatible PD solution to conventional PD solution were included. Groups of biocompatible PD solutions considered were:

- Neutral pH, lactate-buffered, low GDP
- Neutral pH, bicarbonate ($\pm$ lactate) buffered low GDP
- Glucose polymer (icodextrin)
- Combination regimens (e.g. PPEN)

The following types of studies were included:

- Studies of neutral pH, low GDP PD solutions (lactate and bicarbonate $\pm$ lactate buffered) against conventional PD solutions
- Studies of icodextrin against conventional PD solution

Studies of amino acid-based dialysis fluids were excluded.

Types of outcome measures

Primary outcomes

- Decline in RRF (changes in residual creatinine clearance (CrCl), urea clearance, Kt/V, glomerular filtration rate (GFR), and urine output)
- Peritoneal UF (during peritoneal equilibration test and daily UF)
- Peritonitis rate (episodes/y, episode/total patient-months on PD) and incidence (number of events/follow-up period)
- Technique survival (number of participants remaining on PD at study completion)
- Patient survival (number of participants alive at study completion)
- Toxicity/adverse events (e.g. rash, uncontrolled fluid overload)

Secondary outcomes

- Inflow pain
- Changes in peritoneal membrane transport (four-hour dialysate:plasma creatinine)
- Dialysis adequacy (CrCl, Kt/V)
- Hospitalisation (number of hospitalisation days during study follow-up period)

Search methods for identification of studies

Electronic searches

We searched the [Cochrane Kidney and Transplant Specialised Register](#) up to 12 February 2018 through contact with the Information Specialist using search terms relevant to this review. The Specialised Register contains studies identified from:

1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
2. Weekly searches of MEDLINE OVID SP
3. Handsearching of kidney-related journals and the proceedings of major kidney conferences
4. Searching of the current year of EMBASE OVID SP
5. Weekly current awareness alerts for selected kidney and transplant journals
6. Searches of the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

Studies contained in the Specialised Register are identified through search strategies for CENTRAL, MEDLINE, and EMBASE based on the scope of Cochrane Kidney and Transplant. Details of these strategies, as well as a list of handsearched journals, conference

proceedings and current awareness alerts, are available in the Specialised Register section of information about [Cochrane Kidney and Transplant](#).

See [Appendix 1](#) for search terms used in strategies for this review.

Searching other resources

1. Reference lists of review articles, relevant studies and clinical practice guidelines.
2. Letters seeking information about unpublished or incomplete studies to investigators known to be involved in previous studies.

Data collection and analysis

Selection of studies

The review was undertaken by six authors. The search strategy described was used to obtain titles and abstracts of studies that have been relevant to the review. The titles and abstracts were screened independently by two authors. Studies that were not applicable were discarded. Two authors independently assessed retrieved abstracts and, if necessary the full text, of these studies to determine which studies satisfied the inclusion criteria.

Data extraction and management

Data extraction was carried out independently by the same authors using standard data extraction forms. Studies reported in non-English language journals were translated before assessment. Where more than one publication of one study existed, reports were grouped together and the most recent or most complete data set were used. Any discrepancy between published versions was highlighted. Disagreements were resolved by consultation.

Assessment of risk of bias in included studies

The following items were independently assessed by two authors using the risk of bias assessment tool ([Higgins 2011](#)) (see [Appendix 2](#)).

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study?
 - Participants and personnel (performance bias)
 - Outcome assessors (detection bias)
- Were incomplete outcome data adequately addressed (attrition bias)?
- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias?

If a sufficient number of studies (greater than 10) measured the same outcome, thereby assessed to have enough power to detect asymmetry, a funnel plot was performed to evaluate for possible publication bias.

Measures of treatment effect

For dichotomous outcomes (e.g. death, inflow pain, peritonitis) results were expressed as risk ratios (RR) with 95% confidence intervals (CI). Where continuous scales of measurement were used

to assess the effects of treatment (e.g. decline in RRF, urine volume), the mean difference (MD) was used, or the standardised mean difference (SMD) if different scales were used. When data were not presented in a format suitable for inclusion in meta-analysis (e.g. median, interquartile range (IQR)), they were presented in tabulated form.

Unit of analysis issues

For cross-over studies where data were available, only data from the first phase of studies were included.

Dealing with missing data

Any further information required from the original author was requested by written correspondence and any relevant information obtained in this manner was included in the review.

Assessment of heterogeneity

Heterogeneity was analysed using a χ^2 test on N-1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I^2 test (Higgins 2003). I^2 values of 25%, 50% and 75% correspond to low, medium and high levels of heterogeneity.

Assessment of reporting biases

Two authors independently assessed the risk of reporting biases in studies using the risk of bias assessment tool (Higgins 2011).

Data synthesis

Data were summarised using the random-effects model although the fixed-effect model was also analysed to ensure robustness of the model chosen and susceptibility to outliers.

Subgroup analysis and investigation of heterogeneity

Subgroup analysis was performed where feasible to explore possible sources of heterogeneity (e.g. study duration, participants, interventions and study quality). Heterogeneity among participants may have been related to age and renal pathology. Heterogeneity in treatments may have been related to prior agents used and the agent, dose and duration of therapy (Table 1).

Separate analyses were performed for glucose polymer (icodextrin) solutions and glucose-based biocompatible fluids due to anticipated differences in outcomes. For neutral pH low GDP PD solutions, sub-group analyses were performed for lactate-buffered and bicarbonate ($\pm$ lactate) buffered solutions.

Sensitivity analysis

Where sufficient studies were available we investigated the following:

- study duration
- incident versus prevalent patients
- single versus multicentre studies
- parallel versus cross-over design
- PD fluid types
- presence of selection bias
- presence of other significant bias

- weekly residual GFR in patients with baseline GFR > 2 mL/min/1.73 m².

'Summary of findings' tables

We presented the main results of the review in 'Summary of findings' tables. These tables present key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined, and the sum of the available data for the main outcomes (Schünemann 2011a). The 'Summary of findings' tables also included an overall grading of the evidence related to each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach (GRADE 2008; GRADE 2011). The GRADE approach defined the quality of a body of evidence as the extent to which one could be confident that an estimate of effect or association was close to the true quantity of specific interest. The quality of a body of evidence involved consideration of within-trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Schünemann 2011b). We presented the following outcomes in the 'Summary of findings' tables.

Summary of findings (Table 1)

- RRF
- Urine volume (mL/d)
- Peritoneal UF (mL/4 hours)
- Peritoneal solute transport rate (4 hours dialysis:plasma creatinine)
- Peritonitis rate (episodes/total patient-months)
- Technique failure (death-censored)
- Death (all causes)
- Inflow pain and adverse events

Summary of findings (Table 2)

- Uncontrolled fluid overload
- Rash
- RRF
- Urine volume (mL/d)
- Daily UF (mL/d)
- Peritonitis
- Technique failure (death-censored)
- Death (all causes) and adverse events

RESULTS

Description of studies

Results of the search

We searched the Cochrane Kidney and Transplant Register of Studies (12 February 2018) and identified 59 new reports. After full-text assessment 21 new studies were identified. Six new studies (six reports) were included (Cho 2013; Park 2012a; STARCH 2015; Szeto 2015; TRIO 2016; Yoo 2015), 10 (17 reports) were excluded (Chang 2016; Chow 2014; Coester 2006; EDEN 2013; Hiss 2013; IMPENDIA 2013; Lui 2012; Selby 2007a; Yehia 2014; Yoon 2014), and one ongoing study was identified (NCT01228279). Five studies are awaiting assessment (recently completed; no data available/abstract-only publication and awaiting author; unable to access

full-text) (De Los Rios 2016; Do 2006a; Kim 2006; Kocyigit 2015; NCT01753154). We also identified 30 new reports of existing included and excluded studies.

A total of 42 studies (133 reports, 3262 participants) were included, 35 were excluded, 10 are awaiting assessment, and there is one ongoing study (Figure 1).

Figure 1. Flow diagram. * Non-RCTs excluded from the 2018 update

Included studies

Twenty-nine studies (1971 participants) examined the effect of neutral PH, low GDP PD solution against conventional PD solutions (Bajo 2011; balANZ 2010; Cancarini 1998; Carrasco 2001; Choi 2008; Cnossen 2011; Coles 1997; DIUREST 2010; EURO-BALANCE 2004; Fan 2008; Feriani 1998; Fernandez-Perpen 2012; Fusshoeller 2004; Kim 2003; BALNET 2008; Lai 2012a; Mactier 1998; Pajek 2008; Rippe 2001; Schmitt 2002; Szeto 2007; Szeto 2015; Tranaeus 2000; TRIO 2016; Weiss 2009; Yoo 2015; Zeier 2003). Of these, 18 studies (1416 participants) examined lactate-buffered neutral PH, low GDP PD solutions (Bajo 2011; balANZ 2010; Carrasco 2001; Cho 2013; Choi

2008; Cnossen 2011; DIUREST 2010; EURO-BALANCE 2004; Fan 2008; Kim 2003; BALNET 2008; Lai 2012a; Park 2012a; Rippe 2001; Szeto 2007; Szeto 2015; TRIO 2016; Zeier 2003) and 11 studies (555 participants) examined bicarbonate ($\pm$ lactate)-buffered neutral PH, low GDP PD solutions (Cancarini 1998; Coles 1997; Feriani 1998; Fernandez-Perpen 2012; Fusshoeller 2004; Mactier 1998; Pajek 2008; Schmitt 2002; Tranaeus 2000; Weiss 2009; Yoo 2015).

Thirteen studies (1291 participants) compared the clinical outcomes of once daily use of icodextrin with that of conventional PD solution (Bredie 2001; Davies 2003; di Paolo 2000; Finkelstein 2005; Konings 2003; Lin 2009a; MIDAS 1994; Paniagua 2008; Plum

2002; Posthuma 1997; STARCH 2015; Takatori 2011; Wolfson 2002). Of these, three studies examined the effect of icodextrin in patients with high or high average membrane transport characteristics (Davies 2003; Finkelstein 2005; Paniagua 2008).

Excluded studies

A total of 35 studies were excluded from the review. The reasons for exclusion included wrong intervention (e.g. amino acid-based solutions; comparison of two regimes of the same biocompatible

PD solution; comparison of two different types of biocompatible PD solution) or short duration studies.

For this update non-RCTs have been removed.

Risk of bias in included studies

Risk of bias domains of individual studies is presented in Figure 2 and the summary of risk of bias of all the included studies is presented in Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bajo 2011	+	+	?	?	+	+	+
balANZ 2010	+	+	+	?	+	+	?
BALNET 2008	?	?	+	?	+	+	?
Bredie 2001	?	?	?	?	+	+	?
Cancarini 1998	?	?	?	?	+	+	?
Carrasco 2001	+	?	?	?	+	+	?
Cho 2013	?	?	+	?	+	+	?
Choi 2008	?	?	+	?	+	+	?
Crossen 2011	?	?	?	?	?	+	+
Coles 1997	+	?	+	?	+	+	?
Davies 2003	+	+	+	?	+	+	?
di Paolo 2000	?	?	?	?	?	?	?
DIUREST 2010	+	+	+	?	+	+	?
EURO-BALANCE 2004	?	?	+	?	?	+	?
Fan 2008	?	?	+	?	+	+	+
Feriani 1998	+	+	+	?	+	+	?
Fernandez-Perpen 2012	+	+	?	?	+	+	+
Finkelstein 2005	+	+	+	?	+	?	?
Fusshoeller 2004	?	?	+	?	+	+	?
Kim 2003	?	?	+	?	+	+	?

Figure 3. (Continued)

Kim 2003	?	?	+	?	-	-	?
Konings 2003	?	+	+	?	?	+	?
Lai 2012a	-	-	+	?	?	-	-
Lin 2009a	+	+	+	+	?	+	?
Mactier 1998	?	?	+	+	?	?	-
MIDAS 1994	+	+	?	?	?	-	?
Pajek 2008	?	?	+	?	?	+	?
Paniagua 2008	+	?	+	?	-	-	?
Park 2012a	?	?	+	?	-	+	?
Plum 2002	?	?	-	?	?	-	?
Posthuma 1997	?	?	+	?	+	+	?
Rippe 2001	+	+	-	?	-	-	?
Schmitt 2002	?	?	+	?	-	+	?
STARCH 2015	+	+	+	?	+	-	?
Szeto 2007	+	+	+	?	+	+	?
Szeto 2015	+	+	+	?	+	+	-
Takatori 2011	?	?	-	?	?	+	?
Tranaeus 2000	?	?	+	?	-	+	?
TRIO 2016	+	?	+	+	-	+	?
Weiss 2009	+	?	+	?	-	+	?
Wolfson 2002	+	+	+	+	-	-	?
Yoo 2015	+	?	+	?	+	-	?
Zeier 2003	?	?	?	?	-	-	?

Allocation

Random sequence generation

Random sequence generation was judged to be at low risk of bias in 18 studies (balANZ 2010; Carrasco 2001; Coles 1997; Davies 2003; DIUREST 2010; Feriani 1998; Finkelstein 2005; Lin 2009a; MIDAS 1994; Paniagua 2008; Rippe 2001; STARCH 2015; Szeto 2007; Szeto 2015; TRIO 2016; Weiss 2009; Wolfson 2002; Yoo 2015) and at high risk of bias in three studies (Bajo 2011; Fernandez-Perpen 2012; Lai 2012a). The risk of bias was unclear in 21 studies.

Allocation concealment

Allocation concealment was judged to be at low risk of bias in 13 studies (balANZ 2010; Davies 2003; DIUREST 2010; Feriani 1998; Finkelstein 2005; Konings 2003; Lin 2009a; MIDAS 1994; Rippe 2001;

STARCH 2015; Szeto 2007; Szeto 2015; Wolfson 2002) and at high risk of bias in three studies (Bajo 2011; Fernandez-Perpen 2012; Lai 2012a). The risk of bias was unclear in 26 studies.

Blinding

Performance bias (blinding of participants and investigators) was judged to be at low risk of bias in 25 studies (balANZ 2010; BALNET 2008; Cho 2013; Choi 2008; Davies 2003; Fan 2008; Finkelstein 2005; Kim 2003; Konings 2003; Lai 2012a; Lin 2009a; Mactier 1998; Pajek 2008; Paniagua 2008; Park 2012a; Posthuma 1997; Schmitt 2002; STARCH 2015; Szeto 2007; Szeto 2015; Tranaeus 2000; TRIO 2016; Weiss 2009; Wolfson 2002; Yoo 2015) and at high risk of bias in eight studies (Coles 1997; DIUREST 2010; EURO-BALANCE 2004; Feriani 1998; Fussheoeller 2004; Plum 2002; Rippe 2001; Takatori 2011). The risk of bias was unclear in nine studies.

Detection bias (blinding of outcome assessors) was judged to be at low risk of bias in four studies (Lin 2009a; Mactier 1998; TRIO 2016; Wolfson 2002) and was unclear in 38 studies.

Incomplete outcome data

Attrition bias was judged to be at low risk of bias in 10 studies (balANZ 2010; Bredie 2001; Carrasco 2001; Finkelstein 2005; Fusshoeller 2004; Posthuma 1997; STARCH 2015; Szeto 2007; Szeto 2015; Yoo 2015) and at high risk of bias in 21 studies (Bajo 2011; BALNET 2008; Cancarini 1998; Cho 2013; Choi 2008; Coles 1997; Davies 2003; DIUREST 2010; Fan 2008; Feriani 1998; Fernandez-Perpen 2012; Kim 2003; Paniagua 2008; Park 2012a; Rippe 2001; Schmitt 2002; Tranaeus 2000; TRIO 2016; Weiss 2009; Wolfson 2002; Zeier 2003). The risk of bias was unclear in 11 studies.

Patients lost to follow-up ranged from 0% to 83.4%.

Selective reporting

Reporting bias was judged to be at low risk of bias in 23 studies (Bajo 2011; balANZ 2010; BALNET 2008; Choi 2008; Coles 1997; Davies 2003; DIUREST 2010; EURO-BALANCE 2004; Fan 2008; Feriani 1998; Fernandez-Perpen 2012; Konings 2003; Lin 2009a; Pajek 2008; Park 2012a; Posthuma 1997; Schmitt 2002; Szeto 2007; Szeto 2015; Takatori 2011; Tranaeus 2000; TRIO 2016; Weiss 2009) and at high risk of bias in 16 studies (Bredie 2001; Cancarini 1998; Carrasco 2001; Cho 2013; Cnossen 2011; Fusshoeller 2004; Kim 2003; Lai 2012a; MIDAS 1994; Paniagua 2008; Plum 2002; Rippe 2001; STARCH 2015; Wolfson 2002; Yoo 2015; Zeier 2003). The risk of bias was unclear in three studies.

Other potential sources of bias

Seven studies (17%) were identified as high risk for other potential sources of bias (Bajo 2011; Cnossen 2011; Fan 2008; Fernandez-Perpen 2012; Lai 2012a; Mactier 1998; Szeto 2015). The potential sources of bias included mixed use of neutral pH, low GDP solutions from different manufacturers with variable levels of GDP and types of buffers in the intervention group (two studies),

potential centre-related effects (one study), different baseline characteristics between patients in intervention and control groups (three studies), unclear description of participant details (one study). The risk of bias was unclear for all other studies.

Effects of interventions

See: **Summary of findings for the main comparison** Low GDP (all buffer types) compared to standard glucose dialysate for peritoneal dialysis (PD); **Summary of findings 2** Glucose polymer (icodextrin) compared to standard glucose dialysate for peritoneal dialysis (PD)

The studies were analysed using both random effects and fixed effects models and found no difference between the two models. The results presented below therefore refer to those obtained using a random-effects model. Quantitative analyses with high levels of heterogeneity ($I^2 \geq 75\%$) were not reported.

Neutral pH, low GDP versus conventional glucose PD solution

Residual renal function

In high certainty evidence, the use of neutral pH, low GDP solution improved the preservation of RRF (**Analysis 1.1** (15 studies, 835 participants: SMD 0.19, 95% CI 0.05 to 0.33; $I^2 = 0\%$). This approximated to a mean difference in GFR of 0.54 mL/min/1.73m² (95% CI 0.14 to 0.93). This effect was presented for all follow-up duration categories analysed: up to 12 months (**Analysis 1.2** (11 studies, 722 participants): SMD 0.18, 95% CI 0.05 to 0.32; $I^2 = 3\%$), 12 to 24 months (**Analysis 1.3** (10 studies, 641 participants): SMD 0.25, 95% CI 0.10 to 0.41; $I^2 = 0\%$), and more than 24 months (**Analysis 1.4** (6 studies, 343 participants): SMD 0.30, 95% CI 0.08 to 0.51; $I^2 = 0\%$). This translated into MD in GFR of 0.59 mL/min/1.73 m² (95% CI 0.16 to 1.05), 0.71 mL/min/1.73 m² (95% CI 0.28 to 1.16) and 0.85 mL/min/1.73 m² (95% CI 0.23 to 1.44), respectively. Subgroup analysis was performed on PD fluid types (**Analysis 1.5**). This analysis was limited by the fact that the majority of studies used only one solution type (Balance®) such that no useful conclusions could be drawn. There was no evidence of publication bias **Figure 4**.

Figure 4. Funnel plot of comparison: 1 Low GDP (all buffer types) versus standard glucose dialysate, outcome: 1.1 Residual renal function.

Urine volume

In high certainty evidence, daily residual diuresis was higher in PD patients receiving neutral pH, low GDP PD solutions ([Analysis 1.6](#) (11 studies, 791 participants): MD 114.37 mL/d, 95% CI 47.09 to 181.65; $I^2 = 3\%$). There was little or no difference in urine volume up to 12 months follow-up ([Analysis 1.7](#) (10 studies, 819 participants): MD 69.72 mL/d, 95% CI -55.95 to 195.40; $I^2 = 60\%$). The benefit was observed with greater than 1 year follow-up durations: 12 months to 24 months ([Analysis 1.8](#) (8 studies, 579 participants): MD 110.57 mL/d, 95% CI 40.81 to 180.34; $I^2 = 0\%$) and more than 24 months ([Analysis 1.9](#) (3 studies, 279 participants): MD 169.22 mL/d, 95% CI 23.98 to 314.46; $I^2 = 0\%$). Subgroup analysis was performed on PD fluid types ([Analysis 1.10](#)). Again, this analysis was limited by the fact that the majority of trials used only one solution type (Balance®) such that no useful conclusions could be drawn. The proportion of patients who developed anuria was not different between the two groups ([Analysis 1.11](#) (2 studies 246 participants): RR 0.56, 95% CI 0.18 to 1.75; $I^2 = 60\%$).

Peritoneal ultrafiltration

The four-hour peritoneal UF measured during a peritoneal equilibration test may be lower in the neutral pH, low GDP solution group ([Analysis 1.12](#) (9 studies, 414 participants): SMD -0.42, 95% CI -0.74 to -0.10; $I^2 = 51\%$; estimated MD -69.72 mL/4 hours,

95% CI -122.84 to -16.60; low certainty evidence). However, there was a moderate heterogeneity, which could not be explained by differences in study design, study population, or risk of bias. Outcomes from daily peritoneal UF analysis could not be reported due to high heterogeneity ($I^2 = 82\%$).

Peritoneal solute transport rate

The four-hour dialysate:plasma creatinine ratio (D/P_{Creat}) measured during a peritoneal equilibration test may be higher in the neutral pH, low GDP solution group ([Analysis 1.13](#) (10 studies, 746 participants): MD 0.01, 95% CI 0.00 to 0.03; $I^2 = 1\%$; low certainty evidence). However, subgroup analysis with patient characteristics ([Analysis 1.14](#)), fluid types ([Analysis 1.15](#)) and study design ([Analysis 1.16](#)) showed no significant difference in four-hour D/P_{Creat} values between the neutral pH, low GDP solution and control groups.

Peritoneal small solute clearance

Neutral pH low GDP PD solution may make little or no difference to peritoneal creatinine clearance ([Analysis 1.17](#) (7 studies, 510 participants): MD -0.44 L/week/1.73 m², 95% CI -2.03 to 1.15; $I^2 = 0\%$) or peritoneal urea clearance ([Analysis 1.18](#) (6 studies, 422 participants): MD -0.01, 95% CI -0.12 to 0.09; $I^2 = 26\%$; low certainty evidence) between treatments using and conventional PD solution.

Peritonitis

Neutral pH, low GDP and conventional PD solution groups may make little or no difference to the incidence of peritonitis ([Analysis 1.19](#) (12 studies, 1055 participants): RR 1.26, 95% CI 0.92 to 1.72; $I^2 = 69\%$; low certainty evidence). Similarly, there was little or no difference to peritonitis rate ([Analysis 1.20](#) (10 studies, 18,184 patient-months): RR 1.18, 95% CI 0.84 to 1.64; $I^2 = 67\%$; low certainty evidence). A moderate level of heterogeneity was noted for both analyses and when studies were classified according to the risk of attrition bias, the incidence of peritonitis was lower in the neutral pH, low GDP solution group in studies with a low risk for attrition bias ([Analysis 1.21](#) (3 studies, 359 participants): RR 0.65, 95% CI 0.47 to 0.90; $I^2 = 0\%$).

Inflow pain

In very low certainty evidence, it is uncertain whether neutral pH, low GDP solution use led to any differences in may decrease the incidence of inflow pain ([Analysis 1.22](#) (1 study, 58 participants): RR 0.51, 95% CI 0.24 to 1.08). Two additional cross-over RCTs reported significantly lower risk of inflow pain with its use ([Fusshoeller 2004](#); [Mactier 1998](#)). In the study by [Mactier 1998](#), bicarbonate/lactate-buffered PD solution may have had a more favourable effect on inflow pain than purely bicarbonate-buffered PD solution. These latter two cross-over studies were excluded from meta-analysis due to the inability to isolate data from the first arm of the study.

Hospitalisation

In very low certainty evidence, it is unsure whether neutral pH, low GDP PD solutions reduce the duration of hospitalisation ([Analysis 1.23](#) (2 studies, 230 participants): MD 3.02 days, 95% CI -7.08 to 13.12; $I^2 = 45\%$).

Technique failure

In low certainty evidence neutral pH, low GDP PD solutions may make little or no difference to death-censored technique failure, although overall participant numbers were relatively small for assessing this outcome ([Analysis 1.24](#) (15 studies, 1275 participants): RR 1.10, 95% CI 0.75 to 1.63; $I^2 = 0\%$).

Patient survival

In low certainty evidence neutral pH, low GDP PD solutions may make little or no difference to death (all causes), although overall participant numbers were relatively small for assessing this outcome ([Analysis 1.25](#) (15 studies, 1229 participants): RR 0.73, 95% CI 0.47 to 1.14; $I^2 = 0\%$).

Adverse events

In very low certainty evidence, it is uncertain whether neutral pH, low GDP PD solutions use led to any differences in adverse events compared with conventional PD solutions (6 studies, 519 participants) ([balANZ 2010](#); [Coles 1997](#); [EURO-BALANCE 2004](#); [Feriani 1998](#); [Schmitt 2002](#); [Tranaeus 2000](#)) ([Table 2](#)).

Glucose polymer (icodextrin) versus convention glucose PD solution

Peritoneal ultrafiltration

In moderate certainty evidence, icodextrin uniformly augmented peritoneal UF compared with glucose exchanges ([Analysis 2.1](#) (4

studies, 102 participants): MD 448.54 mL/d, 95% CI 289.28 to 607.80; $I^2 = 0\%$). It should be noted that only one of these four studies allowed the use of hypertonic glucose PD solution (3.86%) in the control group ([Finkelstein 2005](#)). In this study of 92 APD patients with higher peritoneal solute transport rate (defined as $D/P_{Creat} > 0.7$) and UF failure (defined as four-hour net UF < 100 mL using 2.5% dextrose), icodextrin resulted in a higher net UF volumes ($+373.8 \pm 58.9$ mL/d) compared with 4.25% dextrose (-239.7 ± 151.0 mL/d) in the controls. Similarly, when the use of icodextrin was compared to 2.5% dextrose PD solution according to the peritoneal equilibration test category, [Lin 2009a](#) reported increases in UF capacities in all patients except low transporters. Patients with higher peritoneal transport characteristics derived greater UF benefit.

Episodes of uncontrolled fluid overload

In moderate certainty evidence, icodextrin probably reduced reported episodes of uncontrolled fluid overload ([Analysis 2.2](#) (2 studies, 100 participants): RR 0.30, 95% CI 0.15 to 0.59; $I^2 = 0\%$).

Residual renal function

In low certainty evidence, icodextrin may make little or no difference to RRF ([Analysis 2.3](#) (4 studies, 114 participants): SMD 0.12, 95% CI -0.26 to 0.49, $P = 0.5$; $I^2 = 0\%$). This approximated to a mean difference in renal CrCl of 0.30 mL/min (95% CI -0.65 to 1.23).

Urine volume

In low certainty evidence, icodextrin-induced increase in peritoneal UF volumes may make little or no difference to daily urine volumes ([Analysis 2.4](#) (3 studies, 69 participants): MD -88.88 mL/d, 95% CI -356.88 to 179.12, $P = 0.5$; $I^2 = 0\%$). Indeed, [Davies 2003](#) reported better maintenance of urine volume with the use of icodextrin at six months when compared to 2.27% dextrose PD solution use ([Analysis 2.5](#)).

Peritoneal small solute clearance

In low certainty evidence, icodextrin may make little or no difference to peritoneal CrCl ([Analysis 2.6](#) (3 studies, 237 participants): SMD 0.36, 95% CI -0.24 to 0.96; $I^2 = 66\%$; estimated MD 0.36 mL/min 95% CI 0.24 to 0.95). Moderate to high heterogeneity was observed and appeared to be related to study design variability. Two studies were open-label in design with unclear description of the number of participants in each peritoneal equilibration test category ([Plum 2002](#); [Posthuma 1997](#)). Similar to their findings with peritoneal UF, [Lin 2009a](#) reported greater peritoneal CrCl measurements in all participants except low transporters.

Peritonitis

In low certainty evidence, icodextrin may make little or no difference to peritonitis incidence ([Analysis 2.7](#) (6 studies, 667 participants): RR 0.95, 95% CI 0.77 to 1.18; $I^2 = 0\%$).

Technique failure

The majority of studies had short follow-up duration (less than six months) and low event numbers. It is uncertain whether icodextrin use led to any differences in technique failure ([Analysis 2.9](#) (4 studies, 350 participants): RR 0.60, 95% CI 0.32 to 1.12, $I^2 = 0\%$; very low certainty evidence).

Patient survival

In the context of low event numbers and short follow-up durations, it is uncertainty whether icodextrin improves patient survival ([Analysis 2.10](#) (6 studies, 816 participants): RR 0.82, 95% CI 0.32 to 2.13; $I^2 = 0\%$; very low certainty evidence).

Adverse events

In low certainty evidence, icodextrin may make little or no difference to the risk of rash compared with glucose exchanges ([Analysis 2.8](#) (3 studies, 755 participants): RR 2.51, 95% CI 0.59 to 10.72; $I^2 = 38\%$). In very certainty evidence, it is uncertain whether icodextrin use led to any differences in adverse events (5 studies, 816 participants) ([Lin 2009a](#); [MIDAS 1994](#); [Paniagua 2008](#); [STARCH 2015](#); [Wolfson 2002](#)) ([Table 2](#)).

DISCUSSION

Summary of main results

This systematic review has demonstrated strong evidence that the use of neutral pH, low GDP PD solution improves preservation of RRF and urine volume compared with conventional PD solution. Its impact on inflow pain was at least comparable if not superior compared to conventional glucose PD solutions. Although the use of neutral pH, low GDP PD solution led to higher D/P_{creat} creatinine and lower UF volume during peritoneal equilibration test, there was a moderate level of heterogeneity affecting analysis of UF. Moderate-to-high heterogeneity was also observed in the analysis examining the risk of peritonitis, such that the effect of neutral pH, low GDP PD solutions on peritonitis currently remains uncertain. However, when the analysis was repeated according to the risk of attrition bias, the incidence of peritonitis was lower using neutral pH, low GDP PD solutions in studies identified at a low risk of attrition bias. Peritoneal small solute clearance was not affected by neutral pH, low GDP PD solutions. Treatment using neutral pH, low GDP solution was not observed to affect death-censored technique failure, duration of hospitalisation and death (all causes), although the event rates were too low to be confident that there was no effect on these outcomes. The use of icodextrin in one PD exchange daily led to increased peritoneal UF volumes and a lower risk of uncontrolled fluid overload compared with glucose PD exchanges alone. These benefits were more pronounced in patients with higher peritoneal solute transport rates and extended to individuals with identified UF failure. The augmentation of peritoneal UF was not associated with any changes in residual renal clearance or urine volume. Icodextrin did not affect peritoneal solute transport rate or peritoneal small solute clearance. It also did not affect technique survival or patient survival, although the event rates and study durations were insufficient to adequately study these outcomes.

Overall completeness and applicability of evidence

The review demonstrated that RRF and urine volume were better preserved with neutral pH, low GDP PD solution than with conventional PD solution. The benefit of RRF preservation was observed in both shorter (≤ 1 year) and longer follow-up durations (> 2 years). The exact mechanism of neutral pH, low GDP solution on preservation of RRF and urine volume remains unclear, however, it is postulated that lower GDP exposure might result in minimisation of GDP-induced tubular damage and apoptosis based on the previously published experimental work published by [Justo 2005](#). Interestingly, the majority of studies analysed used

one particular solution (Balance®, Fresenius Medical Care, Bad Homburg, Germany; [Bajo 2011](#); [balANZ 2010](#); [BALNET 2008](#); [Cho 2013](#); [Choi 2008](#); [EURO-BALANCE 2004](#); [Kim 2003](#); [Park 2012a](#); [Szeto 2007](#); [Szeto 2015](#)), which reportedly contains the lowest level of GDP amongst products available in market ([Jorres 2012](#)).

In contrast to the previous review ([Cho 2014](#)), this update demonstrated lower UF volume with treatment using neutral pH, low GDP PD solution during the four-hour peritoneal equilibration test compared to conventional PD solution. The reduced peritoneal UF with neutral pH, low GDP PD solution could lead to body volume expansion, increased urine volume and augmented RRF ([Bargman 2010](#)). Another potential explanation could be faster decline in RRF resulting from volume depletion from higher peritoneal UF volume in the conventional PD solution group, as reported in the recent analysis of predictors of RRF based on the results from [balANZ 2010](#) ([Htay 2016](#)). Furthermore, it is important to acknowledge the presence of moderate level of heterogeneity, which could not be explained by differences in the study design, study population or risks of bias in included studies. Such observed heterogeneity undermines confidence that neutral pH, low GDP PD solutions alter peritoneal UF.

Moreover, it is also possible that reduced UF capacity in patients receiving neutral pH, low GDP PD solutions could have been the consequence of higher peritoneal solute transport rate (defined as 4-hour dialysate/plasma creatinine ratio), as shown here. These results should also be interpreted with caution as peritoneal solute transport rate was assessed at a single time point at the end of study rather than as longitudinal changes in peritoneal solute transport rate over the study period and so did not take baseline differences into consideration. This is relevant as three studies (30%) in the analyses reported higher baseline peritoneal solute transport rate in patients treated with neutral pH, low GDP PD solutions compared to those who received conventional PD solutions ([balANZ 2010](#); [Lai 2012a](#); [Szeto 2015](#)). Ideally, the effects of types of PD solutions on longitudinal peritoneal solute transport rate trends should be compared rather than comparing the values at a single time point without accounting for inter-individual differences. For example, [balANZ 2010](#) reported peritoneal solute transport rate stability over two years in patients who were treated with neutral pH, low GDP PD solutions as opposed to a progressively rising peritoneal solute transport rate trajectory over time in those who received conventional PD solution ([Johnson 2012](#)).

Another potential benefit of neutral pH, low GDP PD solutions was alleviation of inflow pain. This condition is reported to occur in up to 73% of PD patients receiving conventional PD solutions and has been attributed to their acidic pH ([Vaamonde 1975](#)). The trend towards benefit of neutral pH, low GDP fluids on inflow pain in this study supports the common practice of using these fluids for this clinical indication. Nevertheless, the results of the present review should be interpreted cautiously as the only study included in the meta-analysis was not blinded ([Rippe 2001](#)). Consequently, the results may have been potentially influenced by observer and performance biases. Furthermore, one of the cross-over design studies reported appreciable variation in the frequency of inflow pain amongst the nine participating centres, raising the possibility of confounding centre effects ([Mactier 1998](#)).

A noteworthy finding of this review was the uncertain impact of neutral pH, low GDP fluids on either the proportion of individuals experiencing peritonitis or overall peritonitis rates. This issue

has become highly topical since the (balANZ 2010) reported that neutral pH, low GDP fluid use resulted in a 50% increase in time to first peritonitis episodes and a 36% reduction in overall peritonitis rates compared with conventional solution. The suggested explanation for this finding was improved peritoneal host defence mechanisms, given that there was considerable experimental evidence that neutral pH, low GDP fluids significantly improved viability and function of peritoneal mesothelial cells, leukocytes and macrophages (Boulanger 2002; Jorres 1998; Mortier 2003; Schambye 1996; Topley 1997; Witowski 2005). A similar beneficial effect of biocompatible PD solutions on peritonitis rates had also been reported following extended follow-up in another study (Tranaeus 2000). In contrast, most investigations, which were small and underpowered, found no effect of biocompatible PD solutions on peritonitis risk (Bajo 2011; BALNET 2008; Choi 2008; Coles 1997; DIUREST 2010; Fan 2008; Feriani 1998; Fernandez-Perpen 2012; Park 2012a; Rippe 2001; Szeto 2015; TRIO 2016; Yoo 2015). Perhaps not surprisingly, when all of these studies were combined in a meta-analysis, significant heterogeneity was observed. When this heterogeneity was explored, the main contributing factor appeared to be risk of attrition bias (i.e. due to patient drop-out), such that peritonitis rates were significantly reduced by neutral pH, low GDP PD solutions in studies with low risk of attrition bias due to low drop-out rates (balANZ 2010; Szeto 2015; Yoo 2015). Future well-designed RCTs are warranted to address this relation.

Icodextrin significantly augmented peritoneal UF in both short-term and long-term studies (up to 24 months) and when compared to various concentrations of glucose PD solutions, including hypertonic exchanges. For instance Finkelstein 2005 observed a net change in UF volume of 401.6 ± 79 mL/d in the icodextrin group compared to -6.98 ± 57.2 mL/d in the 4.25% glucose group at two weeks. Importantly, the UF benefit of icodextrin extended to patients with UF failure and was superior to 4.25% glucose PD solution use ($+373.8 \pm 58.9$ mL/d versus -239.7 ± 151.0 mL/d, respectively; Finkelstein 2005). Similarly, subgroup analysis of the two studies (Posthuma 1997; Takatori 2011) with the longest follow-up periods (24 months; Analysis 2.1) showed a MD of 510.55 mL/d (95% CI 10.10 to 1011, $P = 0.05$), in favour of icodextrin. The findings of this systematic review therefore support the recommendations of the International Society for Peritoneal Dialysis (ISPD) Ad Hoc Committee on Ultrafiltration Management in Peritoneal Dialysis that icodextrin should be used in the long dwell of patients who are identified to have high peritoneal solute transport rate or UF failure (Mujais 2000). It also supports the ISPD Cardiovascular and Metabolic Guideline recommendation that “once-daily icodextrin be considered as an alternative to hypertonic glucose PD solutions for long dwells in PD patients experiencing difficulties maintaining euvoalaemia due to insufficient peritoneal UF, taking into account the individual patient’s peritoneal transport state” (Wang 2015).

Given that manipulation of peritoneal UF via various interventions has not infrequently been reported to induce reciprocal changes in urine volume and residual renal clearance measurements (Bargman 2010; Davies 2009), these outcomes were specifically examined in the present review and found not to be compromised by icodextrin-enhanced peritoneal UF.

Similarly, the additional fluid volume removed via the peritoneal cavity with icodextrin was not associated with increased peritoneal small solute clearance measurements. It should be noted however

that moderate to high study heterogeneity was detected, primarily related to variability in the peritoneal membrane transport characteristics of patients included in each study. Indeed, enhancement of small solute clearance with icodextrin use was reported by two studies, with benefit seen only in those individuals with higher peritoneal solute transport rate (Finkelstein 2005; Lin 2009a). Further studies are therefore warranted to examine the effects of icodextrin on peritoneal small solute clearance according to peritoneal transport status.

Reassuringly, icodextrin was not found to be associated with increased harm compared with glucose exchanges alone. Skin rash was the most commonly reported adverse event, which led to cessation of icodextrin in 0% to 4.3% of patients (Finkelstein 2005; Lin 2009a; Wolfson 2002) across the identified studies. However, no study reported occurrence of rash severe enough to warrant hospitalisation or additional therapeutic interventions other than cessation of icodextrin. It is unknown whether any of these patients were subsequently re-challenged using icodextrin. Similarly, six studies reported comparable incidence of adverse events with the use of neutral pH, low GDP PD solutions compared to conventional PD solutions (balANZ 2010; Coles 1997; EURO-BALANCE 2004; Feriani 1998; Schmitt 2002; Tranaeus 2000).

Despite the fact that use of neutral pH, low GDP PD solution was associated with better preservation of RRF and urine volume, its use did not result in improved technique or patient survival compared with conventional PD solution. Given that the numbers of events and included patients in this meta-analysis were relatively small, the review was inadequately powered to examine these hard end-points.

Quality of the evidence

The quality of the present review was suboptimal as many studies failed to specify methods of randomisation, allocation concealment and blinding of outcome assessors. In addition, a considerable number of studies had high risks of attrition bias (50%) and reporting bias (38%). It was often unclear whether data were analysed based on intention-to-treat analysis and how the study dealt with dropouts. In general, studies were limited by small sample size, large dropout numbers, and short follow-up durations, which reduced the strength of the review.

Potential biases in the review process

The strength of this review is that it included an up-to-date and comprehensive systematic review of previous publications through a thorough MEDLINE, EMBASE, and CENTRAL search and included only RCTs or quasi-RCTs, as pre-specified. For cross-over RCTs, in order to minimise the carry-over effect, only the data from the first phase of studies were included for analyses. Data extraction, data analysis, and quality assessment were performed by two independent investigators, and any differences in consensus were checked with an additional two authors. The outcome of peritonitis was examined in terms of both peritonitis rate and incidence of peritonitis to account for non-standardised methods of reporting across studies. However, it should be noted that there is a potential for bias as one of the authors of this review (DJ) was the principal investigator of balANZ 2010 which was included in this review.

Agreements and disagreements with other studies or reviews

This review demonstrated that the use of low GDP PD solution improved preservation of RRF at all study time points. This finding is similar to that of a previous review by [Yohanna 2015](#), who also reported that the benefit of better preservation of RRF with low GDP PD solution was observed even in the early (within six months) follow-up period and at all various study periods. This review also drew a similar conclusion regarding RRF and urine volume preservation as that of [balANZ 2010](#), one of the largest and highest quality RCTs examining the effects of low GDP PD solution on RRF. This study reported that the use of low GDP PD solution was associated with 27% better preservation of RRF and 37% better preservation of urine volume than conventional PD solution, after adjusting for potential confounders ([Htay 2016](#)).

The peritoneal solute transport rate (D/P_{creat}) was significantly higher with the use of low GDP PD solution in the present review. The disparity of this finding compared with that of previous reviews ([Cho 2014](#); [Yohanna 2015](#)) might relate to the fact that peritoneal solute transport rate was assessed at a single time point at the end of study, rather than as longitudinal changes in peritoneal solute transport rate over the study period and so did not take baseline differences into consideration. This finding of the review also contrasted with that of one of the largest RCTs ([balANZ 2010](#)), which compared the longitudinal changes of peritoneal solute transport rate between the two PD solutions and observed that peritoneal solute transport rate was stable in patients treated with low GDP PD solution but was increased in patients treated with conventional PD solution over a two year follow-up period ([Johnson 2012](#)).

The present review also observed lower four-hour peritoneal UF volume measured during a peritoneal equilibration test in patients treated with neutral pH low GDP PD solution compared with those treated with conventional PD solution. This finding was not observed in the previous review. This analysis in the present review suffered a moderate level of heterogeneity which could not be satisfactorily explained and which reduced confidence in the finding.

AUTHORS' CONCLUSIONS

Implications for practice

- In PD patients, treatments using neutral pH, low GDP PD solutions should be used to improve preservation of RRF and urine volume.
- Neutral pH, low GDP PD solutions should also be considered when inflow pain is present.

- Icodextrin use should be used in patients who require an increase in peritoneal UF to achieve optimal fluid status, particularly those with high or high-average membrane transport characteristics.
- The current available evidence is insufficient to accurately determine the effects of neutral pH, low GDP PD solutions or icodextrin on other clinical outcomes including peritonitis, peritoneal solute transport rate, technique survival or patient survival.

Implications for research

- Further studies are needed to adequately determine the effect of neutral pH, low GDP PD solution on patient level-outcomes, such as peritonitis and technique survival. These studies should be adequately powered and of sufficient duration. Studies should only include one type of biocompatible PD solution in the treatment group given variable concentrations of GDP amongst available products. This is particularly relevant when examining the effect on peritonitis as different products using different connectology.
- Specific outcomes to add value would include assessment of longitudinal change in peritoneal solute transport rate rather than an absolute result to assess the trend in peritoneal solute transport rate.
- Future research should be conducted using standard definitions and clearly state co-interventions used if they are likely to influence the measured outcome (e.g. icodextrin and peritoneal UF). A comprehensive list of definitions is available from the ISPD guidelines to guide designing future studies.
- Future appropriately powered studies are needed to examine the effect of icodextrin on hypertension control and cardiovascular endpoints

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES
Characteristics of included studies [ordered by study ID]

Bajo 2011

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: 4 years Follow-up period: 24 months
Participants	<ul style="list-style-type: none"> Country: Spain Setting: multicentre (2 sites), university hospital Incident adult CAPD patients Number: treatment group (13); control group (20) Mean age $\pm$ SD (years): treatment group (62 ± 11); control group (59 ± 15) Sex (M/F): treatment group (10/3); control group (9/11) Exclusion criteria: none
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Balance (Fresenius Medical Care) <p>Control group</p> <ul style="list-style-type: none"> Standard PD fluid (Stay Safe)
Outcomes	<ul style="list-style-type: none"> Peritonitis rate Peritoneal UF (4 hours, 4.25% glucose solution) RRF Patient survival
Notes	<ul style="list-style-type: none"> Supported by grants from RETICS from Instituto de Salud Carlos III and unrestricted grant from Fresenius Medical Care

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "patients were alternately assigned to either 'balance' or standard PD fluid depending on the time point of inclusion"
Allocation concealment (selection bias)	High risk	Quote: "patients were alternately assigned to either 'balance' or standard PD fluid depending on the time point of inclusion"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement

Bajo 2011 (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	High drop-out rate: 21/33 (63.6%)
Selective reporting (reporting bias)	Low risk	All relevant outcomes reported
Other bias	High risk	Outcome parameters significantly different at baseline (e.g. urine volume, RRF)

balANZ 2010

Methods	<ul style="list-style-type: none"> Study design: open-label, parallel RCT Study duration: November 2004 to September 2010 Follow-up period: 24 months
Participants	<ul style="list-style-type: none"> Countries: Australia, New Zealand, Singapore Setting: multicentre (16 sites) Adult PD patients ≥ 18 and < 81 years (either CAPD or APD); diagnosis of ESKD; first treatment for ESKD by any dialysis modality within 90 days prior to or following enrolment (patients may be enrolled prior to commencing first treatment if there is clear indication that the treatment modality is CAPD or APD and they consent in advance to enter the study); selected to be treated by CAPD or APD; residual GFR at enrolment ≥ 5 mL/min/1.73 m², urine volume/d ≥ 400 mL at enrolment; written informed consent before any study related activities; ability to understand the nature and requirements of the study Number: treatment group (91); control group (91) Mean age $\pm$ SD (years): treatment group (59.3 $\pm$ 14.2); control group (57.9 $\pm$ 14.7) Sex (M/F): treatment group (52/39); control group (48/43) Exclusion criteria: prognosis for survival < 12 months; pregnancy or lactation period; history of malignancy other than a successfully and completely treated cutaneous squamous cell or basal cell carcinoma or carcinoma in-situ of the cervix within the last 5 years; any acute infections at the time of enrolment; any disease of the abdominal wall, such as injury or surgery, burns, hernia, dermatitis, that in the opinion of the Investigator would preclude the patient from being able to have PD; any inflammatory bowel diseases (Crohn's disease, ulcerative colitis or diverticulitis) that in the opinion of the Investigator would preclude the patient from being able to have PD; any intra-abdominal tumours or intestinal obstruction; active serositis; any condition (mental or physical) that would interfere with the patient's ability to comply with the study protocol; known or suspected allergy to study product or related products; participation in any other clinical study where an intervention is designed to moderate rate of change of RRF
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH, low GDP dialysis solution (Balance) <p>Control group</p> <ul style="list-style-type: none"> Conventional dialysis solution (StaySafe) for a period of 2 years
Outcomes	<p>Primary outcome</p> <ul style="list-style-type: none"> Slope of RRF decline measured as GFR (mean of renal urea and CrCl) over time (follow-up 24 months) <p>Secondary outcomes</p> <ul style="list-style-type: none"> Time from initiation of PD to anuria (daily urine volume < 100 mL) Peritoneal small solute clearance (Kt/V, CrCl) Peritoneal transport status (PET D/P creatinine and D/Do glucose)

balANZ 2010 (Continued)

- Peritoneal UF capacity (mL/d) and UF (mL/day/m²)
- Technical survival
- Patient survival
- Peritonitis rates
- Adverse events

Notes • Study funded by Fresenius Medical Care

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "To ensure adequate concealment of allocation, randomization was performed using a central computer and web-based link to the central database, with stratification according to centre and the presence or absence of diabetic nephropathy"
Allocation concealment (selection bias)	Low risk	Quote: "To ensure adequate concealment of allocation, randomization was performed using a central computer and web-based link to the central database, with stratification according to centre and the presence or absence of diabetic nephropathy"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "An open-label study", but unlikely to have influenced the objective outcomes measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Drop-out rate 3/185 (1.6%), balanced between groups
Selective reporting (reporting bias)	Low risk	All relevant clinical parameters reported
Other bias	Unclear risk	Insufficient information to permit judgement

BALNET 2008

Methods	<ul style="list-style-type: none"> • Study design: open-label, parallel RCT • Study recruitment period: June 2004 to May 2006 • Follow-up period: 12 months (24-month follow-up result in abstract form available)
Participants	<ul style="list-style-type: none"> • Country: South Korea • Setting: multicentre (4 sites) • Incident adult patients > 18 years commencing on CAPD • Number: treatment group (48); control group (43) • Mean age ± SD (years): treatment group (55.3 ± 13.2); control group (52.8 ± 13.6) • Sex (M/F): treatment group (31/17); control group (24/19)

BALNET 2008 (Continued)

- Exclusion criteria: mechanical problems with PD catheter; expected kidney transplantation within 12 months; life expectancy < 6 months; plans to transfer to another hospital; dialysis required due to acute renal failure; patient refusal

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Low-GDP solution (Balance) <p>Control group</p> <ul style="list-style-type: none"> Conventional PD solution <p>After 4-week run-in phase on conventional fluid, each group started CAPD with the designated PD solution</p>
Outcomes	<p>Primary end point</p> <ul style="list-style-type: none"> GFR defined by the mean of renal urea and CrCl <p>Secondary end points</p> <ul style="list-style-type: none"> Urine volume Survival: patient survival, technique survival and peritonitis-free survival Clinical laboratory data: peritoneal solute transport rate represented by dialysate-to-plasma ratio for creatinine at 4h (D/P Cr) and blood chemistry
Notes	<ul style="list-style-type: none"> Partly supported by Fresenius Korea

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "open-labelled, randomised, prospective study" However, unlikely to have influenced the objective outcomes measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropout rate, 22/91 (24.1%), 5/48 patients in low GDP group switched to HD - no reason specified that may have been relevant to the therapy they had received
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Bredie 2001

Methods	<ul style="list-style-type: none"> Study design: cross-over RCT Study duration: not reported Follow-up period: 6 weeks during each arm (overall 3 months)
Participants	<ul style="list-style-type: none"> Country: Netherlands Setting: single centre, university hospital Prevalent adult patients on CAPD; established on CAPD for at least 3 months, using 3 to 4 standard exchanges/24 h; free of peritonitis and mechanical drainage complications for at least 3 months prior to their inclusion Number: 21 Mean age $\pm$ SD: 50.3 $\pm$ 11.8 years Sex (M/F):15/6 Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 7.5% icodextrin in place of glucose-containing fluid for the overnight dwell <p>Control group</p> <ul style="list-style-type: none"> Standard glucose-containing PD fluid (1.36%, 2.27%, 3.86%) for the overnight dwell <p>Patients performed CAPD with both control and treatment fluids for a period of 6 weeks each</p>
Outcomes	<ul style="list-style-type: none"> Peritonitis
Notes	<ul style="list-style-type: none"> Funding received from Rijnstate Hospital Arnhem and Baxter Healthcare Company, Benelux

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Drop-out rate: 1/22 (5%)
Selective reporting (reporting bias)	High risk	Limited clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Cancarini 1998

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: not reported Follow-up period: 2 months
Participants	<ul style="list-style-type: none"> Country: Italy Setting: multicentre (2 sites) Prevalent adult patients on CAPD Number: treatment group (16); control group (17) Mean age $\pm$ SD: 64 $\pm$ 11 years Sex (M/F): 15/18 Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 33 mmol/L bicarbonate PD solution <p>Control group</p> <ul style="list-style-type: none"> Standard 40 mmol/L lactate PD solution
Outcomes	<ul style="list-style-type: none"> BP Biochemistry - serum bicarbonate, albumin, total protein concentrations
Notes	<ul style="list-style-type: none"> Other clinical parameters (e.g. peritonitis, UF) not reported. However, the primary aim of the study was evaluate the effect on biochemistry Author contacted, awaiting response

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Open label, however unlikely to have affected outcome
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Drop-out rate of 7/33 (21.2%). Reason for dropout not reported
Selective reporting (reporting bias)	High risk	Limited reporting of outcomes
Other bias	Unclear risk	Insufficient information to permit judgement

Carrasco 2001

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: not reported Follow-up period: 3 months
Participants	<ul style="list-style-type: none"> Country: Spain Setting: multicentre (4 sites) Prevalent adult CAPD patients Number: treatment group (20); control group (11) Age, range (years): treatment group (58.8, 23 to 76); control group (56.7, 34 to 79) Sex (M/F): treatment group (9/11); control group (5/6) Exclusion criteria: antibiotics during the previous 30 days; serious illnesses (e.g. requiring hospitalisation during the previous 30 days); HIV positive; pregnancy or lactating; bicarbonate supplementation into PD fluids or orally
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 25 mmol/L bicarbonate/15 mmol/L lactate PD solution <p>Control group</p> <ul style="list-style-type: none"> Standard 35 mmol/L lactate PD solution
Outcomes	<ul style="list-style-type: none"> Venous plasma bicarbonate concentrations Vital signs
Notes	<ul style="list-style-type: none"> This was a study primarily examining the ability of the new bicarbonate/lactate PD solutions on improving acidosis in PD patients Author contacted, awaiting response Funding received from Baxter Healthcare Ltd

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation (3 patients/block)
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Open label, however, unlikely to have affected measured outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs
Selective reporting (reporting bias)	High risk	Limited reporting of clinical outcomes

Carrasco 2001 (Continued)

Other bias	Unclear risk	Insufficient information to permit judgement
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Cho 2013

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: April 2001 to December 2003 Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> Country: Republic of Korea Setting: multicentre (2 sites) Incident adult CAPD patients Exclusion criteria: Severe systemic disease including liver cirrhosis, SLE, rheumatoid arthritis, inflammatory bowel disease, vasculitis and malignancy
Interventions	Treatment group <ul style="list-style-type: none"> Low-GDP solution (Balance solution, Fresenius Medical Care) Control group <ul style="list-style-type: none"> Conventional solution (StaySafe, Fresenius Medical Care)
Outcomes	<ul style="list-style-type: none"> UF volume RRF 24-hour peritoneal UF Urine volume solute clearance glucose absorption inflammatory markers nutritional status
Notes	<ul style="list-style-type: none"> Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	open-label, unlikely to affect the outcomes of study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias)	High risk	24% dropout

Biocompatible dialysis fluids for peritoneal dialysis (Review)

Cho 2013 (Continued)

All outcomes

Selective reporting (reporting bias)	High risk	limited outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Choi 2008

Methods	<ul style="list-style-type: none"> Study design: open parallel RCT Study duration: not reported Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> Country: Korea Setting/ study design: single centre, university hospital Prevalent adult patients on CAPD; maintained on CAPD for at least 6 months prior to study enrolment using standard PD fluids, and considered to be adequately dialysed; patients used three or four 1.5 to 2.5 L exchanges/d Number: treatment group (51); control group (53) Mean age $\pm$ SD (years): treatment group (52.6 $\pm$ 12.4); control group (55.4 $\pm$ 11.9) Sex (M/F): treatment group (20/31); control group (27/26) Exclusion criteria: dialysis-related complications (e.g. CAPD peritonitis, exit-site infection, tunnel infection) within the previous 8 weeks; more than 2 episodes of peritonitis within the previous 6 months
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH, low GDP solution (Balance; Fresenius Medical Care) <p>Control group</p> <ul style="list-style-type: none"> Standard PD solution
Outcomes	<ul style="list-style-type: none"> Urine volume Death (due to causes unrelated to PD) 4-hour dialysate:plasma creatinine Change in D:P Cr over the study period Peritoneal UF Change in peritoneal UF Kt/V urea (renal, peritoneal and total) CrCl (renal, peritoneal and total)
Notes	<ul style="list-style-type: none"> Funding received from Yonsei University College of Medicine, the Korean Society of Nephrology and Fresenius Medical Care

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement

Choi 2008 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label design thus no blinding of investigators or participants. However, unlikely to have impacted on objective clinical outcomes (e.g. urine volume)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Large number of patients voluntarily changed to the low GDP PD solution (36/104 (35%)). Per protocol analysis
Selective reporting (reporting bias)	Low risk	All appropriate outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Cnossen 2011

Methods	<ul style="list-style-type: none"> Study design: open, parallel RCT Study duration: not reported Follow-up period: 3 months
Participants	<ul style="list-style-type: none"> Country: Germany, Netherlands Setting: multicentre (2) Prevalent adult patients on CAPD Number: treatment group (12); control group (11) Mean age $\pm$ SD (years): treatment group (70.0 $\pm$ 13.1); control group (55.3 $\pm$ 15.6) Sex (M/F): treatment group (9/3); control group (10/1) Exclusion criteria: intercurrent infection; use of 1.1% amino acids (Nutrineal, Baxter Healthcare); treatment with APD
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH, low GDP solution (Physioneal; Baxter Healthcare) <p>Control group</p> <ul style="list-style-type: none"> Standard PD fluid (Dianeal, Baxter Healthcare)
Outcomes	<ul style="list-style-type: none"> Advanced glycation end product concentrations RRF
Notes	<ul style="list-style-type: none"> Significant disparity in baseline age between the two groups noted. Author contacted, awaiting response

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement

Cnossen 2011 (Continued)

Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Low drop-out rate (3/26 (11.5%))
Selective reporting (reporting bias)	High risk	Limited reporting of clinical outcomes
Other bias	High risk	A large difference in baseline age between the treatment and control groups raise concern for inadequate randomisation

Coles 1997

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: not reported Follow-up period: 2 months, with optional 4 month extension period
Participants	<ul style="list-style-type: none"> Countries: UK, Italy Setting: multicentre (5) Prevalent adult patients on CAPD for at least 3 months; receiving Dianeal PD4 for at least 1 month; RRF of ≤ 5 mL/min; weekly (renal + peritoneal) CrCl of ≥ 50 L/1.73 m² RRF ≥ 5 mL/min; using 4 or 5, 2 litre bags/24 hours with no dry period Number: treatment group 1 (20); treatment group 2 (20); control group (19) Age, range (years): treatment group 1 (54.5, 21.6 to 73.7); treatment group 2 (54.8, 27.8 to 79.1); control group (58.4, 25.5 to 74.7) Sex (M/F): treatment group 1 (17/3); treatment group 2 (13/7); control group (10/9) Exclusion criteria: low peritoneal transport (4-hour dialysate:plasma creatinine < 0.5); known to be HIV positive; peritonitis within the previous 30 days; suffered from liver disease or diabetes mellitus; added medication routinely to the dialysis bag
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Bicarbonate-buffered (38 mmol/L bicarbonate) dialysis fluid <p>Treatment group 2</p> <ul style="list-style-type: none"> Bicarbonate/lactate-buffered (25 mmol/L bicarbonate, 15 mmol/L lactate) dialysis fluid <p>Control group</p> <ul style="list-style-type: none"> Conventional lactate-buffered (40 mmol/L lactate) dialysis fluid
Outcomes	<ul style="list-style-type: none"> Peritoneal UF at 2 months Peritonitis Abdominal pain

Biocompatible dialysis fluids for peritoneal dialysis (Review)

Coles 1997 (Continued)

- Other adverse events

Notes

- Funding received from Baxter Healthcare Corporation, Brussels, Belgium

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation in groups of 3, done separately for each centre; actual method of randomisation not reported
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open label. Measured outcome (e.g. abdominal pain) may have been influenced by lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Drop-out 13/59 (22%). Unequal between three groups with peritonitis being the major cause which may have been due to the treatment received
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Davies 2003

Methods

- Study design: parallel RCT
- Study duration:
- Follow-up period: 6 months

Participants

- Countries: Germany, Sweden, UK
- Setting: multicentre (number not reported)
- Prevalent adult patients > 18 years on APD or CAPD; uncontrolled hypertension (BP > 140/90 mmHg), treated hypertension, or a dialysis prescription with a daily average glucose concentration of $\geq 2.27\%$; high or high-average peritoneal solute transport (corrected 4h D/P creatinine ratio ≥ 0.65); urine output ≤ 750 mL/d; patient tolerance of a dialysis regimen with a long dwell of ≥ 6 hours with 2.27% glucose with fill volume of 1.5 to 2.5 L; able to give written informed consent; on PD for at least 90 days
- Number: treatment group (28); control group (22)
- Mean age $\pm$ SD (years): treatment group (56 ± 15); control group (54 ± 15)
- Sex (males): treatment group (54%); control group (45%)
- Exclusion criteria: received icodextrin or other non-glucose solutions in the 30 days before randomisation; treated for peritonitis in the 30 days before randomisation; considered noncompliant; considered to have hypertension despite being clinically volume depleted; use of a 1.36% glucose solution for each exchange; allergy to starch; glycogen storage disease; life expectancy < 12 months; serious illness or injury in the 30 days before randomisation that would invalidate study entry; participation in another interventional study; pregnant or lactating; significant psychiatric disorder that would interfere with their ability to provide informed consent and/ or comply with the study procedures

Davies 2003 (Continued)

Interventions	Treatment group <ul style="list-style-type: none"> 7.5% icodextrin for the long dwell Control group <ul style="list-style-type: none"> 2.27% glucose (Dianeal) for the long dwell
Outcomes	<ul style="list-style-type: none"> Decline in RRF (change in urine output) Change in peritoneal UF volume
Notes	<ul style="list-style-type: none"> Funded by Baxter Healthcare

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from Methods section of paper: "Randomised 1:1 with stratification for centre/country, dialysis modality (CAPD or APD), and presence of cardiovascular disease or LVH"
Allocation concealment (selection bias)	Low risk	Quote from Methods section of paper: "The treatment codes were supplied to study sites in sealed envelopes, which were checked at the end of the study"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote from Methods section of paper: "Identity of the long-dwell solution blinded to patients, investigators and clinical monitors; specially created packaging was used to conceal which solution was which solution was which"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Drop-out rate 20% (10/50). Quote from Results section of paper: "Additional withdrawals from the 2.27% glucose group were for UF failure and patient preference"
Selective reporting (reporting bias)	Low risk	All relevant outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

di Paolo 2000

Methods	<ul style="list-style-type: none"> Study design: cross-over RCT Study duration: not reported Follow-up period: 3 months
Participants	<ul style="list-style-type: none"> Country: Italy Setting: single centre CAPD patients with clinical signs such as hypotension and hyperhydration Number: 9 Mean age (range): 72.5 years (50 to 83) Sex (M/F): 6/3

di Paolo 2000 (Continued)

- Exclusion criteria: not reported

Interventions	<ul style="list-style-type: none"> • Night dwell (> 6 hours) of icodextrin <p>Cross-over design, with two study periods of 3 months each, separated by a 2 week wash out period</p>
Outcomes	<ul style="list-style-type: none"> • Arterial BP
Notes	<ul style="list-style-type: none"> • The study was reported in abstract form only, with BP the only clinical endpoint reported. Data from the first arm of the cross-over study was unable to be isolated. Attempts to contact the authors for further information were unsuccessful due to inability to find contact details

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Unclear risk	Insufficient information to permit judgement

DIUREST 2010

Methods	<ul style="list-style-type: none"> • Study design: open, parallel RCT • Study duration: 1999 to 2005 • Follow-up period: 18 months
Participants	<ul style="list-style-type: none"> • Country: Germany, France, Austria • Setting: multicentre (23 sites) • Adult patients on CAPD or APD aged 18 to 80 years; ESKD, GFR ≥ 3 mL/min (arithmetic mean of renal urea and CrCl) or ≥ 6 mL/min (CrCl) as measured by 24-hour urine collection • Number: treatment group (44); control group (36) • Mean age $\pm$ SD (years): treatment group (52 ± 12); control group (53.8 ± 14.6) • Sex (M/F): treatment group (36/18); control group (14/12) • Exclusion criteria: pregnant or breastfeeding; severe peritonitis episodes; cancer; positive for hepatitis B, hepatitis C and HIV

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DIUREST 2010 (Continued)

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Received either Gambosol trio, a multi-compartment bag with minimal amounts of GDPs (3, 4-DGE < 1 µM) <p>Control group</p> <ul style="list-style-type: none"> Standard PD fluids from different manufacturers in single compartment bags, all containing 3,4-DGE (13-20 µM)
Outcomes	<ul style="list-style-type: none"> RRF (arithmetic mean of renal creatinine and urea clearance) Assessment of fluid balance (body weight, 24-hour urine volume) Serum parameters (CRP, total protein, albumin, electrolytes and phosphate) CA125 in PD effluent Assessment of peritoneal membrane transport characteristics Medications (e.g. BP medications, diuretics and phosphate binders)
Notes	<ul style="list-style-type: none"> Sponsored by Gambro

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from Methods section of paper: "Randomization was performed by means of a centrally managed list based on a table of random numbers in blocks of four and stratified for the presence of diabetes"
Allocation concealment (selection bias)	Low risk	Quote from Methods section of paper: "Randomization was performed by means of a centrally managed list based on a table of random numbers in blocks of four and stratified for the presence of diabetes"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote from Methods section of paper: "... open, parallel study". As fluid balance is one of the main outcomes assessed, risks influencing co-intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	High drop-out rate (41/80 (51.3%)), imbalance between the number of dropouts from each arm. Per protocol analysis
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

EURO-BALANCE 2004

Methods	<ul style="list-style-type: none"> Study design: open, cross-over design and parallel arms Study duration: not reported Follow-up: 12 weeks
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EURO-BALANCE 2004 (Continued)

Participants	<ul style="list-style-type: none"> Country: 11 European countries Setting: multicentre (22 sites) Prevalent adult patients on PD Number: treatment group (36); control group (35) Median age, IQR (years): treatment group (61, 46-68); control group (57, 51-71) Sex (M/F): treatment group (19/7); control group (23/12) Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH, low GDP dialysate (Balance) <p>Control group</p> <ul style="list-style-type: none"> Conventional dialysate <p>Patients received 12 weeks of treatment with both solutions</p>
Outcomes	<ul style="list-style-type: none"> 4-four dialysate:plasma creatinine Kt/V CrCl UF Urine volume Peritonitis rate Adverse events (including inflow pain)
Notes	<ul style="list-style-type: none"> Study funded by Fresenius Medical Care

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Specific randomisation technique not reported. Quote: "After the run-in phase, patients were randomized (1:1) to either ..."
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study with subjective outcome measure such as inflow pain was one of the assessed parameters
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropout rate: 15/86 (17%). Although per protocol analysis performed, the reasons for dropout from initial study group is balanced after excluding the reasons that are unlikely to be dialysis related (e.g. transplantation, flare-up of vasculitis)
Selective reporting (reporting bias)	Low risk	All relevant outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Fan 2008

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: 1 January 2004 to 31 December 2005 Follow-up: 12 months
Participants	<ul style="list-style-type: none"> Country: UK Setting: single centre Incident adult patients on APD or CAPD Number: treatment group (57); control group (61) Mean age $\pm$ SD (years): treatment group (51.6 $\pm$ 2); control group (54.5 $\pm$ 1.7) Sex (M/F): treatment group (38/19); control group (39/22) Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Biocompatible solution (Physioneal or Balance depending on the connectology that was felt to be best suited to the individual) <p>Control group</p> <ul style="list-style-type: none"> Standard PD solution (Dianeal or Stay Safe depending on the connectology that was felt to be best suited to the individual)
Outcomes	<ul style="list-style-type: none"> RRF (assessed by 24-h urine collection) Peritonitis rate PD technique survival Changes in peritoneal membrane function using PET Biomarker of inflammation, CRP
Notes	<ul style="list-style-type: none"> Differences in connectology may have influenced the peritonitis risk. Baxter group also allowed to use Nutrineal/Icodextrin

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding of investigators or participants. However, unlikely to have impacted on objective clinical outcomes (e.g. urine volume)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropout rate of 21.2% (25/118). Not all accounted for with many under "did not complete". Reason unclear

Fan 2008 (Continued)

Selective reporting (reporting bias)	Low risk	All relevant outcomes reported
Other bias	High risk	Issue of connectology and allowance of Nutrineal/icodextrin usage in patients who used Baxter System. Multiple types of PD solutions used in both intervention and control groups

Feriani 1998

Methods	<ul style="list-style-type: none"> Study design: parallel, open label RCT Study duration: not reported Follow-up period: 24 weeks
Participants	<ul style="list-style-type: none"> Countries: Germany Setting: multicentre (14 sites) Adult patients on CAPD (prevalent) who were free of peritonitis for at least 4 weeks preceding the study commencement. Phase II study (24 weeks) <ul style="list-style-type: none"> Number: treatment group (37); control group (36) Median age, range (years): treatment group (54.5, 18.6-78); control group (55, 21.27-79.4) Sex (M/F): treatment group (17/20); control group (20/16) Exclusion criteria: not reported
Interventions	Treatment group <ul style="list-style-type: none"> 34 mmol/L bicarbonate-buffered solution Control group <ul style="list-style-type: none"> 35 mmol/L lactate-buffered PD solution
Outcomes	<ul style="list-style-type: none"> RRF UF Subjective assessment - symptoms Adverse events
Notes	<ul style="list-style-type: none"> Grant from Fresenius Phase I study data only available from conference abstract 36 patients left at the end of phase I of study - no explanation provided

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised centrally and separately for each study centre and block randomisation in steps of four used
Allocation concealment (selection bias)	Low risk	No specific information provided. However central randomisation with probable low risk of selection bias
Blinding of participants and personnel (performance bias)	High risk	Open label, may have affected symptom assessment

Feriani 1998 (Continued)

All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Large number of participants missing between two phases of study that are not accounted for in the paper: 18/123 (14.6%) for 12 weeks; 4/73 (5.5%) for 24 week study
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Fernandez-Perpen 2012

Methods	<ul style="list-style-type: none"> Study design: prospective RCT, presumed open-label (not disclosed) Study duration: not reported Follow-up period: 24 months
Participants	<ul style="list-style-type: none"> Countries: Spain Setting: multicentre (2 university hospitals) Incident patients who are able and willing to perform CAPD with no expressed indication for APD Number: treatment group (11); control group (20) Mean age $\pm$ SD (years): treatment group (68.22 $\pm$ 8.8); control group (59 $\pm$ 15) Sex (M/F): treatment group (8/3); control group (9/11) Diabetic: treatment group (38%); control group (15%) Exclusion criteria: none
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> BicaVera (1.5, 2.3%, 4.25% glucose) <p>Control group</p> <ul style="list-style-type: none"> Conventional PD fluid (Stay-safe; 1.5%, 2.3% and 4.25%)
Outcomes	<ul style="list-style-type: none"> Peritonitis rate Death Technique survival UF capacity RRF
Notes	<ul style="list-style-type: none"> Study supported by grants from REDinREN, MLC and unrestricted grant from Fresenius Medical Care. Note: significant difference in outcome re: UF capacity and RRF reported, but these differences were present from the baseline

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "patients were randomly assigned to either BicaVera or the standard PD fluid by the doctors"

Fernandez-Perpen 2012 (Continued)

Allocation concealment (selection bias)	High risk	Quote: "patients were randomly assigned to either BicaVera or the standard PD fluid by the doctors"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	High dropout rate (23 /31 (74.2%)). Imbalance in missing data between the two groups
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	High risk	Outcome parameters significantly different at baseline (e.g. urine volume, RRF)

Finkelstein 2005

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: 1 July 2001 to 11 October 2003 Follow-up period: 2 weeks
Participants	<ul style="list-style-type: none"> Countries: Australia, USA Setting: multicentre (number not reported) Adult patients ≥ 18 years on APD with peritoneal membrane transport characteristics in the high-average or high category; high or high average peritoneal transport characteristics (4-hour dialysate:plasma creatinine > 0.70 and 4-hour D/D_0 glucose < 0.34) based on the results of the screening PET; receiving treatment with APD using HomeChoice (Baxter) or HomeChoice PRO (Baxter) cyclers for at least 30 days before the baseline visit; stable on their PD prescription before the screening visit; using an APD prescription for at least 3 days before the baseline visit that included a long-dwell exchange with duration of 12 to 16 hours and fill volume of 2.0 to 2.5 L of a 4.25% dextrose solution; stable health; able to tolerate a 12 to 16 hour long dwell; free from peritonitis for at least 45 days before use of the study solution Number: treatment group (47); control group (45) Mean age $\pm$ SD (years): treatment group (50.1 ± 2.1); control group (53.3 ± 1.8) Sex (M/F): treatment group (28/19); control group (28/17) Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 7.5% icodextrin (Extraneal; Baxter) for the long dwell <p>Control group</p> <ul style="list-style-type: none"> 4.25% dextrose solution (Dianeal PD-2; Baxter) for the long dwell
Outcomes	<ul style="list-style-type: none"> UF Small solute clearances Adverse events (rash)

Finkelstein 2005 (Continued)

- Notes
- Study funded by Baxter Healthcare Corporation, which also manufactured the double-blind product

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Centrally maintained randomisation list
Allocation concealment (selection bias)	Low risk	Centrally maintained randomisation list
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind - use of identical solution bags
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropout rate: 7/92 (8%), balanced between groups
Selective reporting (reporting bias)	Unclear risk	All relevant outcomes within the short time frame reported
Other bias	Unclear risk	Insufficient information to permit judgement

Fusshoeller 2004

Methods	<ul style="list-style-type: none"> Study design: open, cross-over RCT Study duration: not reported Follow-up period: 12 months (6 months in each phase)
Participants	<ul style="list-style-type: none"> Country: Germany Setting: single centre, university Adult patients on APD Number: 14 Mean age $\pm$ SD: 40.0 $\pm$ 10.7 years Sex (M/F): 4/10 Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH bicarbonate/ lactate buffered PD solution (Physioneal; Baxter Healthcare) <p>Control group</p> <ul style="list-style-type: none"> Conventional PD solution (Dianeal; Baxter Healthcare) <p>Patients completed 6 months of APD using either control or treatment PD solution, followed by a further 6 months of APD using the alternative PD solution</p>

Fusshoeller 2004 (Continued)

Outcomes	<ul style="list-style-type: none">Inflow pain	
Notes	<ul style="list-style-type: none">Funding source: not reported	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded. This is particularly relevant as 'inflow pain' was reported as one of the outcomes in unblinded state
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropout rate: 2/14 (14%)
Selective reporting (reporting bias)	High risk	Primary outcome of interest of this study related to peritoneal macrophages and inflammatory markers. No other clinical parameter was reported - including peritonitis, survival, RRF
Other bias	Unclear risk	Insufficient information to permit judgement

Kim 2003

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: not reported Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> Country: South Korea Setting: multicentre (2 hospitals) Incident adult patients on CAPD Number: treatment group (16); control group (10) Mean age $\pm$ SD (years): treatment group (51.6 $\pm$ 3.6); control group (56.1 $\pm$ 5.2) Sex (M/F): not reported Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Low GDP PD solution (pH 7.0, two compartment bag, StaySafe Balance solution; Fresenius Medical Care) <p>Control group</p>

Kim 2003 (Continued)

- Standard glucose-containing dialysis fluid (pH 5.5, single compartment bag, stay-safe; Fresenius Medical Care)

Outcomes	<ul style="list-style-type: none"> • RRF • Peritoneal transport (4-hour dialysate:plasma creatinine)
Notes	<ul style="list-style-type: none"> • Funding received from Fresenius Medical Care Korea and Medical Research Institute grant, Kyungpook National University Hospital (1998)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement, stratified for diabetes mellitus
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label, however unlikely to have influenced the objective outcome measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropout rates - 38/64 (59%). Missing participants not accounted for. Per protocol analysis
Selective reporting (reporting bias)	High risk	No report of peritonitis or survival
Other bias	Unclear risk	Insufficient information to permit judgement

Konings 2003

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT • Study duration: • Follow-up period: 4 months
Participants	<ul style="list-style-type: none"> • Country: The Netherlands • Setting: multicentre • Prevalent adult patients on CAPD and APD • Number: treatment group (22); control group (18) • Mean age $\pm$ SD (years): treatment group (52.7 ± 10.9); control group (56.4 ± 11.6) • Sex (M/F): treatment group (14/8); control group (14/8) • Exclusion criteria: recent complications (e.g. peritonitis, malignancy, surgery); type I diabetes mellitus; congestive heart failure or coronary artery disease (defined as NYHA class III and higher)
Interventions	Treatment group

Konings 2003 (Continued)

- 7.5% icodextrin in place of glucose-containing fluid for the overnight dwell (patients on CAPD) or the daytime dwell (patients on APD)

Control group

- Standard glucose-containing PD fluid

Outcomes	<ul style="list-style-type: none"> • Technique failure • Peritonitis • Other adverse events (exfoliative dermatitis) • Peritoneal UF • Residual renal GFR • Urine output
Notes	<ul style="list-style-type: none"> • Funding received from Baxter Healthcare • Performed baseline characteristics as if ITT but performed as per protocol for the outcome assessment

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Low risk	"Randomized with the use of sealed envelopes"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open label - but unlikely to have influenced objective outcomes measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropout 20% (8/40), but all accounted for. Per protocol analysis
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Lai 2012a

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT • Study duration: commenced July 2003 • Follow-up period: average 3.6 years
Participants	<ul style="list-style-type: none"> • Country: Hong Kong • Setting: multicentre (4 sites) • Incident adult patients on CAPD

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Lai 2012a (Continued)

- Number: treatment group (58); control group (67)
- Mean age $\pm$ SD (years): treatment group (56.4 ± 1.6); control group (59.5 ± 1.35)
- Sex (M/F): treatment group (36/22); control group (33/34)
- Exclusion criteria: malignancy; systemic lupus erythematosus; chronic valvular or congenital heart disease

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • low-GDP PDFs, Gambrosol Trio, Physioneal 40 and Balance <p>Control group</p> <ul style="list-style-type: none"> • Conventional PD Solutions - lactate-buffered glucose based Dianeal PD-2 or ANDY-Disc
Outcomes	<p>Composite co-primary outcomes</p> <ul style="list-style-type: none"> • biochemical profile of cytokines, growth factors, adipokines, and cardiac biomarkers determined after stable PD treatment for an average duration of 2.3 years • dialysis adequacy determined by GFR and daily urine output at initiation and at the time of census after stable PD for an average duration of 3.6 years <p>Also determined</p> <ul style="list-style-type: none"> • UF • Urine volume • Dialysis Adequacy (Kt/V, CrCl) • Residual GFR • 4-hour dialysate:plasma creatinine
Notes	<ul style="list-style-type: none"> • Study supported in part by a Renal Discoveries-International Society of Nephrology grant and a Baxter extramural grant • Randomisation and recruitment into this study unusual. Patients were informed only at 2.3 years after starting their 'study' of their participation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Random assignments were made by the patient's training nursing officer at the individual renal centre
Allocation concealment (selection bias)	High risk	Random assignments were made by the patient's training nursing officer at the individual renal centre
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label, however unlikely to have affected the objective outcomes measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Per protocol analysis

Lai 2012a (Continued)

Selective reporting (reporting bias)	High risk	Peritonitis not reported
Other bias	High risk	<p>Although baseline characteristics were reported to be similar. The paper did not disclose the duration of PD that these patients received, so one cannot exclude that they may represent different vintage.</p> <p>Also, for biochemical analyses, there is no baseline value available, thus it is difficult to be certain whether differences are present truly or due to type I error</p> <p>Multiple types of PD solutions used in intervention and control groups.</p>

Lin 2009a

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: not reported Follow-up period: 4 weeks
Participants	<ul style="list-style-type: none"> Country: China Setting: multicentre (7 sites) Prevalent CAPD patients ≥ 18 years stable during at least 90 days; a minimum of 6 L of daily 2.5% Di-aneal PD-2 or PD-4 dialysate with a night dwell above 8 hours; night dwell volume of 2 L for a minimum of 30 days before inclusion Number: treatment group (98); control group (103) Mean age $\pm$ SD (years): treatment group (56.8 ± 13.5); control group (55.4 ± 14.0) Sex (M/F): treatment group (51/47); control group (45/58) Exclusion criteria: documented anaphylaxis with icodextrin; concomitant chronic diseases such as hepatitis, malignancy, severe cardiac disease; ongoing infection or known infection within the last 30 days; planned or ongoing pregnancy; participation in another clinical or drug study concurrently
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 7.5% icodextrin in night dwell <p>Control group</p> <ul style="list-style-type: none"> 2.5% glucose (Dianeal) in night dwell
Outcomes	<ul style="list-style-type: none"> Changes of peritoneal CrCl (mL/min) Changes of UF volume Metabolic parameters (fasting blood glucose, cholesterol, and triglycerides)
Notes	<ul style="list-style-type: none"> Additional information obtained from author

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was done using a computer program that generated numbers instead of treatment assignments"; block randomisation, using a 1:1 ratio

Lin 2009a (Continued)

Allocation concealment (selection bias)	Low risk	Quote: "Envelopes that contained the number corresponding to the dialysate regimen were held by personnel not directly involved with the study, and could be opened only in an emergency"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Neither doctors nor patients knew the dialysate regimen"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Neither doctors nor patients knew the dialysate regimen"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Low dropout rate, 18/201 (8.9%)
Selective reporting (reporting bias)	Low risk	All relevant clinical outcome parameters are reported
Other bias	Unclear risk	Insufficient information to permit judgement

Mactier 1998

Methods	<ul style="list-style-type: none"> Study design: cross-over RCT Study duration: not reported Follow-up period: three study visits within 1-3 week period
Participants	<ul style="list-style-type: none"> Countries: UK, Sweden Setting: multicentre (8 sites) Prevalent adult patients on CAPD ≥ 18 years and experienced repeated infusion pain that based on medical judgement was not related to the catheter or excessive intraperitoneal volume of dialysis fluid Number: 18 Mean age: 63.5 years Sex (M/F): not reported Exclusion criteria: peritonitis within the previous 30 days
Interventions	<p>Patients evaluated during two dialysis exchanges with each test solution in random order. Thus, all patients underwent six separate study dwells, with a maximum of 2 test evaluations in 1 day, but it was required that these study exchanges were separated by a routine dwell (40 mM lactate solution) of at least 4 hours. All dwells for at least 3 hours, using 3.86% glucose solutions. Solutions used:</p> <ol style="list-style-type: none"> Lactate - Dianeal PD4 Bicarbonate Bicarbonate/lactate
Outcomes	<ul style="list-style-type: none"> Pain scores Adverse symptoms
Notes	<ul style="list-style-type: none"> Large variation within the 8 participating centres in the frequency of inflow pain. Mean frequency was 1/25 (range 1/3 to 1/66) patients

Risk of bias

Mactier 1998 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	1/18 (5.6%) lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Limited reporting of outcomes, but given short duration of study, not possible
Other bias	High risk	Large variation within the 8 participating centres in the frequency of inflow pain

MIDAS 1994

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: March 1991 to February 1992 Follow-up period: 6 months
Participants	<ul style="list-style-type: none"> Country: UK Setting: multicentre (11 sites) Prevalent adult patients on CAPD ≥ 18 years or older and established on CAPD for at least 3 months using standard 3 to 4 exchanges, with no more than one hypertonic (3.86% glucose) bag/24 hours; free of peritonitis and mechanical drainage complications for at least one month prior to the study Number: treatment group (103); control group (106) Mean age $\pm$ SD (years): treatment group (55 ± 15); control group (55 ± 14) Sex (M/F): treatment group (67/36); control group (71/35) Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 7.5% icodextrin as overnight dwell <p>Control group</p> <ul style="list-style-type: none"> Standard glucose-containing PD fluid as overnight dwell
Outcomes	<ul style="list-style-type: none"> Death (all causes) Peritonitis rate Peritoneal UF

MIDAS 1994 (Continued)

Notes

- Study supported by ML Laboratories plc and conducted by Innovata Biomed Limited

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "telephone from a single office (Innovata Biomed) at the first visit"
Allocation concealment (selection bias)	Low risk	Quote: "telephone from a single office (Innovata Biomed) at the first visit"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Although mod-high dropout rate (71/209 (34%)), all missing participants are accounted for and reasonably balanced in terms of cause
Selective reporting (reporting bias)	High risk	RRF not reported
Other bias	Unclear risk	Insufficient information to permit judgement

Pajek 2008

Methods	<ul style="list-style-type: none"> • Study design: open label, cross-over RCT • Study duration: not reported • Follow-up period: 6 months
Participants	<ul style="list-style-type: none"> • Country: Slovenia • Setting: single-centre, University hospital • Prevalent CAPD patients (adult), treated with Dianeal solution for at least 3 months and > 18 years • Number: 21 • Mean age $\pm$ SD: 54.3 $\pm$ 12.4 years • Sex (M/F): 13/8 • Exclusion criteria: peritonitis episode in the last 3 months; a history of or current systemic inflammatory disease or immunomodulatory therapy; HIV, HBV or HCV positivity or other chronic infectious disease; malignant disease; acute exacerbation of heart failure in the last 3 months prior to inclusion in the study
Interventions	<ul style="list-style-type: none"> • After 1-month run-in phase with the Dianeal solution (D solution), patients were randomised (1:1) to either 3 months of treatment with the D solution (group D-P) or to 3 months of treatment with Physioneal 40 (P solution; group P-D) • After 3 months, patients switched therapies to receive a further 3 months of treatment
Outcomes	<p>Primary endpoint</p> <ul style="list-style-type: none"> • Daily UF

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Pajek 2008 (Continued)

Secondary endpoints

- Overnight UF of a timed 10-hour dwell
- 4-hour UF with 2.27% solution on PET
- Low-molecular-weight solute peritoneal transport rates expressed as a D/P for creatinine ratio and D/D1 for glucose ratio
- Peritoneal urea and CrCl
- Residual GFR

Notes

- Study partly supported by a grant from the Slovenian Research Agency and partly by a grant from Baxter Healthcare, Ljubljana, Slovenia. One of the authors is employed by Baxter Healthcare

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement other than, quote: "patients were randomized (1:1)"
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "open-label, randomized". However, unlikely to have influenced the measured objective outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropout rate - 5/26 (19.2%). Per protocol analysis
Selective reporting (reporting bias)	Low risk	All relevant outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Paniagua 2008

Methods	<ul style="list-style-type: none"> • Study design: open label, parallel RCT • Study recruitment: October 2004 to January 2005 • Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> • Country: Mexico • Setting: multicentre (4 sites) • Adult prevalent CAPD patients; diabetes mellitus; high and high average peritoneal transport status • Number: treatment group (30); control group (29) • Mean age $\pm$ SD (years): treatment group (58.9 ± 7.9); control group (60.5 ± 9.3) • Sex (M/F): treatment group (12/18); control group (16/13) • Exclusion criteria: seropositive for hepatitis B or HIV; malignancies; receiving immunosuppressive medications; peritonitis episode within 1 month of screening period

Paniagua 2008 (Continued)

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 7.5% icodextrin in the long dwell <p>Control group</p> <ul style="list-style-type: none"> At least 1 bag with 2.5% glucose in the long dwell <p>Liberal use of 2.5% or 4.25% glucose was allowed in both groups in order to reach treatment goals.</p> <p>Dietary sodium intake prescription was 50 mmol/d for both groups</p>
Outcomes	<p>Primary outcomes</p> <ul style="list-style-type: none"> Improvement in peritoneal UF Reduction in extracellular fluid volume Improvement in metabolic control <p>Secondary outcomes</p> <ul style="list-style-type: none"> Hospitalisations Therapy-related complications
Notes	<ul style="list-style-type: none"> Financial support from Baxter, SA de RL, Mexico

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: Assignment was in a 1:1 ratio through a central randomisation centre
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label study. However, unlikely to have influenced the objective outcomes measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	23 participants dropped out. It is also unclear if 23 were out of 59, or the 82 participants to start with. Per protocol analysis
Selective reporting (reporting bias)	High risk	Limited reporting of clinical outcomes
Other bias	Unclear risk	Insufficient information to permit judgement

Park 2012a

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: October 2005 to April 2007
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Biocompatible dialysis fluids for peritoneal dialysis (Review)

Park 2012a (Continued)

	<ul style="list-style-type: none"> Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> Country: Republic of Korea Setting: multicentre (7 sites) Incident CAPD patients Number: treatment group (79); control group (67) Mean age $\pm$ SD (years): treatment group (52.2 ± 11.4); control group (52.6 ± 11.1) Sex (M/F): treatment group (37/42); control group (30/37) Exclusion criteria: deemed to have $< 80\%$ likelihood of survival for at least 1 year; any malignancy other than treated skin carcinoma; uncontrolled congestive heart failure; recent (within 60 days) myocardial infarction or cerebrovascular accident; active systemic vasculitic disease including SLE, polyarteritis nodosa; anti-neutrophil cytoplasmic antibody-nephritis, active rheumatoid disease or active venous thrombotic-embolic disease; any acute infection at the time of enrolment; active or actively treated tuberculosis or recent (within 30 days); systemic bacterial infection
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH, low GDP PD solution (Balance solution, Fresenius Medical Care) <p>Control group</p> <ul style="list-style-type: none"> Conventional PD solution (Stay-safe, Fresenius Medical Care)
Outcomes	<ul style="list-style-type: none"> inflammation and endothelial dysfunction RRF Urine output 4-hour dialysate:plasma creatinine Peritoneal small solute clearance Peritoneal UF peritonitis rate
Notes	<ul style="list-style-type: none"> The study was supported in part by Fresenius Medical Care, Korea, and also in part by a grant of the Korea Healthcare Technology R&D Project, Ministry for Health and Welfare, Republic of Korea (A084001)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label, unlikely to affect outcomes of study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Overall 23% dropout

Park 2012a (Continued)

Selective reporting (re-reporting bias)	Low risk	All relevant outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Plum 2002

Methods	<ul style="list-style-type: none"> Study design: open label, parallel RCT Study duration: January 1997 to February 1998 Follow-up period: 14 weeks
Participants	<ul style="list-style-type: none"> Countries: Germany, France; Belgium Setting: multicentre (8 sites) Adult prevalent APD patients who had been treated with APD for at least 90 days before the screening visit and whose standard prescription included a long dwell daytime exchange of 2L of 2.27% glucose PD4. Excluded patients with any dry period. Number: treatment group (20); control group (19) Mean age, range (years): treatment group (46.1, 27 to 74); control group (45.5, 26 to 75) Sex (M/F): treatment group (13/6); control group (17/3) Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> 7.5% icodextrin as daytime dwell <p>Control group</p> <ul style="list-style-type: none"> Daytime dwell of Dianeal 2.27%
Outcomes	<ul style="list-style-type: none"> Solute transport - peritoneal urea and CrCl, RRF Fluid balance - net UF, BP, body weight Adverse events
Notes	<ul style="list-style-type: none"> Two diabetic patients in each group Funded by Baxter

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label, could have affected introduction of co-intervention affecting the fluid balance measurement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement

Biocompatible dialysis fluids for peritoneal dialysis (Review)

Plum 2002 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Per protocol analysis; 6/39 (15.4%) lost to follow-up
Selective reporting (reporting bias)	High risk	Peritonitis not reported
Other bias	Unclear risk	Insufficient information to permit judgement

Posthuma 1997

Methods	<ul style="list-style-type: none"> Study design: open label, parallel RCT Study duration: February 199 to December 1996 Follow-up period: 24 months 	
Participants	<ul style="list-style-type: none"> Country: Netherlands Setting: single centre Adult prevalent (and some presumed incident) CCPD patients Number: treatment group (19); control group (19) Mean age, range (years): treatment group (49, 32 to 71); control group (56, 21 to 68) Sex (M/F): not reported Exclusion criteria: women of childbearing potential were excluded unless taking adequate contraceptive precautions 	
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> icodextrin for the daytime dwell (14 to 16 hours) <p>Control group</p> <ul style="list-style-type: none"> glucose-containing solution as daytime dwell 	
Outcomes	<ul style="list-style-type: none"> Death Peritonitis Body weight RRF UF Urine volume Serum creatinine CrCl Weight 	
Notes	<ul style="list-style-type: none"> Partially supported by ML laboratories There are 13 publications associated with this study Due to variable follow-up, number of assessed patients in publications differ 	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement

Posthuma 1997 (Continued)

Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open label, unlikely to have influenced the objective outcomes measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropout rate of 34% (13/38) at 24 months, but all accounted for and balanced
Selective reporting (reporting bias)	Low risk	All relevant outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Rippe 2001

Methods	<ul style="list-style-type: none"> Study design: open label, parallel RCT Study duration: not reported Follow-up period: 24 months (initially planned for 12 month study, extended to 24 months without additional patient recruitment)
Participants	<ul style="list-style-type: none"> Country: Denmark, Sweden Setting: multicentre (5 centres) Adult incident and prevalent CAPD patients, > 18 years, able to use 2L bags with a calcium concentration of 1.35 mmol/L Number: treatment group (40); control group (40) Mean age, range (years): treatment group (58, 28 to 80); control group (57, 26 to 82) Sex (M/F): treatment group (25/15); control group (30/10) Exclusion criteria: seropositive for hepatitis B or HIV; malignancy; pregnant
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> neutral pH, low GDP PD solution <p>Control group</p> <ul style="list-style-type: none"> Gambrosol 40 CAPD solution
Outcomes	<ul style="list-style-type: none"> Personal dialysis capacity (PDP) used as a tool to: <ul style="list-style-type: none"> Assess peritoneal transport characteristics Evaluate RRF UF following overnight dwell using 2.5% Dialysate markers - e.g. CA125, hyaluronan, PICP, PIINP Infusion pain
Notes	<ul style="list-style-type: none"> Supported by Gambro Pain assessment not blinded

Biocompatible dialysis fluids for peritoneal dialysis (Review)

Rippe 2001 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Central randomisation office (stratified randomisation with respect to patient age (< 55, > 55 years), diabetes (using insulin or not), and time on PD (< 9 months, > 9 months))
Allocation concealment (selection bias)	Low risk	Not reported but presume low risk given central randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Open-label". During pain assessment phase, no blinding took place which may have affected patient response
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	Although all dropouts accounted for, extremely high proportion (67/80, 83.75%) did not complete the study duration
Selective reporting (reporting bias)	High risk	RRF not reported
Other bias	Unclear risk	Insufficient information to permit judgement

Schmitt 2002

Methods	<ul style="list-style-type: none"> Study design: open cross-over RCT Study duration: not reported Follow-up period: 12 weeks
Participants	<ul style="list-style-type: none"> Countries: Austria, France, Germany Setting: multicentre (6 specialised paediatric dialysis units) Prevalent paediatric patients < 18 years on APD with an average peritoneal fill volume close to 1000-1100 mL/m² BSA Number: 28 Median age (range): 6.0 years (range 0.6 to 15.7) Sex (M/F): 19/9 Exclusion criteria: severe chronic pulmonary, cardiac, hepatic or malignant disease; history of peritonitis in the previous 3 weeks; clinical evidence of major peritoneal adhesions
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH PD fluid (34 mM bicarbonate, BicaVera 170/180/190; Fresenius Medical Care) <p>Control group</p> <ul style="list-style-type: none"> Conventional PD fluid (35 mL lactate, pH 5.5, CAPD 17/18/19; Fresenius Medical Care) <p>Patients performed their usual APD regimen with either the control or treatment fluid for 12 weeks. After a 4 week washout period they completed 12 weeks of APD using the alternative fluid</p>

Schmitt 2002 (Continued)

Outcomes	<ul style="list-style-type: none"> Peritonitis rate, relapsing peritonitis rate Other adverse events (acute fluid overload, aggravated hypertension, severe hyperparathyroidism) Residual GFR 24-hour UF Peritoneal transport (4-hour dialysate:plasma creatinine)
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Notes	<ul style="list-style-type: none"> Funding received from Fresenius Medical Care (Bad Homburg, Germany)
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label, however, unlikely to have influenced the objective outcome measures reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	High dropout rate (12/28, 43%), unclear during which phase of treatment the dropouts occurred. Per protocol analysis
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

STARCH 2015

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: October 2009 to February 2013 Follow-up period: 3 months
Participants	<ul style="list-style-type: none"> Country: Brazil Setting: multicentre (7 sites) Prevalent APD patients Number: treatment group (33); control group (27) Mean age $\pm$ SD (years): treatment group (51.6 ± 16.6); control group (52.2 ± 16.4) Sex (M/F): treatment group (14/19); control group (12/15) Exclusion criteria: not willing to participate in the study; Charlson Index of > 7 or a life expectancy of < 1 year at baseline; positive HIV serology; peritonitis episode preceding the randomisation by 1 month; any hospitalisation due to cardiovascular, metabolic or infectious disease in the month preceding randomisation; any known active cancer, pregnancy; known allergy to starch; a total Kt/V of < 1.7 following the initial change in the prescription

STARCH 2015 (Continued)

Interventions	Treatment group <ul style="list-style-type: none"> Icodextrin solution 2L per day Control group <ul style="list-style-type: none"> Conventional dextrose solution
Outcomes	<ul style="list-style-type: none"> Glucose control Urine volume UF Peritonitis rate Hospitalisation rate Technique failure rate
Notes	<ul style="list-style-type: none"> "This was an investigator-driven clinical trial funded by Baxter Healthcare after approval of the Clinical Evidence Council. The sponsor did not participate in interpretation of results and in preparation of manuscript"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Centralized randomisation schedule in coordinating centre with Random allocation software
Allocation concealment (selection bias)	Low risk	Centralized randomisation using random allocation software
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label, unlikely to affect outcome
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	11% dropout rate
Selective reporting (reporting bias)	High risk	limited outcomes of study reported
Other bias	Unclear risk	Insufficient information to permit judgement

Szeto 2007

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: not reported Follow-up: 12 months
Participants	<ul style="list-style-type: none"> Country: Hong Kong Setting: single centre

Biocompatible dialysis fluids for peritoneal dialysis (Review)

Szeto 2007 (Continued)

- Incident adult patients on CAPD
- Number: treatment group (25); control group (25)
- Mean age $\pm$ SD (years): treatment group (60.9 ± 11.2); control group (55.0 ± 13.7)
- Sex (M/F): treatment group (16/9); control group (14/11)
- Exclusion criteria: unlikely to survive; planned to have elective living-related kidney transplant or transfer to other renal centre within 6 months

Interventions	Treatment group <ul style="list-style-type: none"> • Neutral pH (lactate buffered), low GDP dialysate (Balance; Fresenius) Control group <ul style="list-style-type: none"> • Conventional dialysate
Outcomes	<ul style="list-style-type: none"> • Total Kt/V • Residual GFR • UF • Urine output • Length of hospitalisation • Technique failure • Death (all causes)
Notes	<ul style="list-style-type: none"> • Study partially funded by Fresenius Medical Care

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomized by drawing sealed envelopes, which were prepared and then maintained by a third party not involved in the conduction of the study"
Allocation concealment (selection bias)	Low risk	Quote: "randomized by drawing sealed envelopes, which were prepared and then maintained by a third party not involved in the conduction of the study"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Open-label", but unlikely to have influenced the objective outcomes measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported other than for Subjective global assessment - trained observers were blinded from treatment group allocation and biochemical results of the patients
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropout rate: 2/50 (4%)
Selective reporting (reporting bias)	Low risk	All relevant outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Szeto 2015

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: February 2011 to July 2013 Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> Country: Hong Kong Setting: single centre Incident CAPD patients Number: treatment group (31); control group (33) Mean age $\pm$ SD (years): treatment group (62.9 ± 12.1); control group (57.7 ± 9.9) Sex (M/F): treatment group (17/14); control group (13/20) Exclusion criteria: patients who were unlikely to survive; planned to have elective living-related kidney transplant; planned to transfer to other renal centre within 6 months
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH, low GDP PD solution (Balance solution) <p>Control group</p> <ul style="list-style-type: none"> Conventional PD solution (StaySafe)
Outcomes	<ul style="list-style-type: none"> Fluid status Body composition Nutritional status and arterial stiffness Urine output RRF Peritoneal small solute clearance Peritoneal UF 4-hour dialysate:plasma creatinine Peritonitis rate Hospitalisation
Notes	<p>"This study was supported in part by the Fresenius Medical Care, and CUHK research account 6901031. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript"</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Using a standard randomisation table
Allocation concealment (selection bias)	Low risk	Randomised by third party using randomisation table
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label, unlikely to affect outcome
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement

Szeto 2015 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	9% dropout rate
Selective reporting (reporting bias)	Low risk	All relevant outcomes reported
Other bias	High risk	Different in baseline characteristic between two groups

Takatori 2011

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: May 2005 to April 2007 Follow-up: 24 months
Participants	<ul style="list-style-type: none"> Country: Japan Setting: multicentre (23 sites) Adult incident PD patients (CAPD/APD) with ESKD because of diabetic kidney disease Number: treatment group (21); control group (20) Mean age $\pm$ SD (years): treatment group (55.9 ± 11.16); control group (56.5 ± 9.86) Sex (M/F): treatment group (14/7); control group (13/7) Exclusion criteria: age < 18 years or > 80 years; urine volume < 400 mL/d; urinary tract obstruction due to neoplasm; neurogenic bladder; pregnancy; previous renal replacement therapies including PD, HD and kidney transplantation
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Treated with a maximum of 6 L of daily 1.5% or 2.5% Dianeal PD-2 or PD-4 in association with an overnight or daytime dwell of 2 or 1.5 L of 7.5% icodextrin-containing solution <p>Control group</p> <ul style="list-style-type: none"> Treated with a maximum of 8 L of daily 1.5% or 2.5% Dianeal PD-2 or PD-4 (Baxter)
Outcomes	<p>Primary outcome</p> <ul style="list-style-type: none"> Rate at 2 years of PD technical survival <p>Secondary outcomes</p> <ul style="list-style-type: none"> Rate of decline in RRF <ul style="list-style-type: none"> fluid status measured using body weight, BP, cardiothoracic ratio on CXR, UF volume RRF measured with daily urine volume renal CrCl, weekly Kt/V measured at baseline, 3, 6, 12, 18 and 24 months from the initiation of PD Status of lipid and glucose metabolism <ul style="list-style-type: none"> haemoglobin A1c, glycoalbumin, LDL-cholesterol, HDL-cholesterol, triglycerides
Notes	<ul style="list-style-type: none"> Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement

Takatori 2011 (Continued)

Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "open-label multicenter clinical trial". Given fluid balance is one of the major outcomes assessed, unblinded nature may have influenced introduction of co-intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	High dropout rate - 18/41 (43.9%). However, the majority of dropouts (12) were due to reaching the primary endpoint (i.e. fluid overload), presence of attrition bias for other outcomes cannot be excluded
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Tranaeus 2000

Methods	<ul style="list-style-type: none"> Study design: open parallel RCT Study duration: not reported Follow-up period: 6 months with elective 6 month extension period
Participants	<ul style="list-style-type: none"> Countries: Europe, UK Setting: multicentre (17 sites) Prevalent adult patients on CAPD for at least 3 months, and being treated with 40 mmol/L lactate dialysate (Dianeal PD4) using an integrated disconnect system (Twin-bag) for at least 1 month; normalised (to BSA) GFR of ≤ 7 mL/min/1.73 m² (average of urea and CrCl) using 4 to 5.2-2.5 L exchanges/d, 7 days/wk, with no dry period; total weekly CrCl ≥ 55 L/ 1.73 m² BSA Number: treatment group (70); control group (36) Mean age, range (years): treatment group (55.1, 26.0 to 77.0); control group (56.6, 23.0 to 76.0) Sex (M/F): treatment group (42/28); control group (18/18) Exclusion criteria: acute or chronic exit site or tunnel infection; completed a course of antibiotics for exit site/ tunnel infection or peritonitis in the previous 30 days; other serious illnesses including the need for hospitalisation in the previous 30 days; HIV positive; pregnant or lactating; adding bicarbonate to bags or taking bicarbonate orally
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Bicarbonate-lactate buffered (25 mmol/L bicarbonate, 15 mmol/L lactate, pH 7.4) dialysis solution <p>Control group</p> <ul style="list-style-type: none"> Standard lactate-buffered (40 mmol/L lactate) dialysis solution (Dianeal PD4)
Outcomes	<ul style="list-style-type: none"> Peritoneal UF Dialysis adequacy Peritonitis
Notes	<ul style="list-style-type: none"> Funding received from Baxter Healthcare, Ltd

Tranaeus 2000 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Open-label", however, unlikely to have influenced the objective outcomes measured
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	18/106 (17%) at 6 months; 13/57 (23%) at 12 months, dropout rate at 12 months not accounted for. Overall drop-out rate 62/106 (58.5%)
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

TRIO 2016

Methods	<ul style="list-style-type: none"> Study design: RCT Study duration: August 2005 to July 2010 Follow-up period: 24 months
Participants	<ul style="list-style-type: none"> Countries: Canada and Hong Kong Setting: multicentre Incident adults CAPD or APD patients Number: treatment group (51); control group (50) Mean age $\pm$ SD (years): treatment group (59.9 $\pm$ 11); control group (59.0 $\pm$ 11) Sex (M/F): treatment group (29/22); control group (31/19) Exclusion criteria: unlikely to continue PD for at least 6 months
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Neutral pH, low GDP PD solution (Gambrosol Trio solution) <p>Control group</p> <ul style="list-style-type: none"> Conventional PD solution (Dianeal solution)
Outcomes	<ul style="list-style-type: none"> RRF Urine output 4-hour dialysate:plasma creatinine Peritoneal small solute clearance Peritoneal UF

Biocompatible dialysis fluids for peritoneal dialysis (Review)

TRIO 2016 (Continued)

- peritonitis rate

Notes

- "The Trio Trial was partially funded by an unrestricted grant from Gambro Lundia AB, Lund, Sweden. TS, GW, MT, DO, and PT conceived, designed, and supervised the Trio Trial. TS, SM, AS, and MA conducted the statistical analysis"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Standard computerized algorithm
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label, unlikely to have major impact on outcomes of study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Unlikely to effect the outcomes of study
Incomplete outcome data (attrition bias) All outcomes	High risk	33% dropout rate
Selective reporting (reporting bias)	Low risk	All outcomes of study were reported
Other bias	Unclear risk	Insufficient information to permit judgement

Weiss 2009

Methods

- Study design: cross-over RCT
- Study duration: not reported
- Follow-up period: 24 weeks (+ pain assessment phase, but duration not specified)

Participants

- Countries: Sweden, Netherlands, Switzerland
- Setting: multicentre (16 sites)
- Adult prevalent CAPD patients with no PD-related complications during the previous month.
- Number: all patients (53); full set analysis (27); pain assessment analysis set ()
- Mean age $\pm$ SD (years): all patients (60.9 ± 14.8); full set analysis (56.0 ± 16.8); pain assessment analysis set (58.7 ± 16.4)
- Sex (M/F): all patients (31/22); full set analysis (16/11); pain assessment analysis set (15/8)
- Exclusion criteria: not reported

Interventions

- Patients randomly assigned to two groups, starting with either standard lactate-buffered PD fluid (SPDF) for 12 weeks (phase 1) and switching to bicarbonate-buffered PD fluid (bicPDF) for another 12 weeks (phase 2), or vice versa
- After completing the biocompatibility study phase, pain assessment was performed to allow blinded administration of the solutions (4 exchanges - two with SPDF and two with bicPDF)

Weiss 2009 (Continued)

Outcomes	<ul style="list-style-type: none"> • Biocompatibility markers in effluent and serum <ul style="list-style-type: none"> ◦ Cancer antigen 125 ◦ hyaluronic acid ◦ tumour necrosis factor-alpha ◦ interleukin-6 ◦ vascular endothelial growth factor ◦ interferon gamma ◦ transforming growth factor-beta1 ◦ high-sensitivity C-reactive protein • RRF - GFR • Total fluid loss - peritoneal UF and urine volume in 24 hours • Peritoneal function - dialysate-to-plasma ratios of creatinine and urea • Acid-base parameters • Acid-base parameters • Pain assessment during exchange using McGill pain questionnaire
Notes	<ul style="list-style-type: none"> • Study was supported by Fresenius Medical Care

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A centralized randomization procedure was applied stratifying for diabetes status and time on PD"
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "open-label study", however during pain assessment phase the treatment was instituted in blinded manner. Other measured parameters are objective and unlikely to have been affected
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	High dropout rate, 19/53 (35.8%). Although all missing participants accounted for, but not reported at what stage. Difficult to be certain how many patients completed each phase of the study. Four patients did not participate in pain assessment phase and reasons not provided
Selective reporting (reporting bias)	Low risk	All relevant clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Wolfson 2002

Methods	<ul style="list-style-type: none"> • Study design: open parallel RCT • Study duration: not reported • Follow-up period: 4 weeks - efficacy; 52 weeks - safety
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Wolfson 2002 (Continued)

Participants	<ul style="list-style-type: none"> Countries: Canada, USA Setting: multicentre (32 - efficacy; 42 - safety) Adult prevalent PD patients (CAPD only for efficacy; APD/CAPD for safety) with standard dialysis prescription for at least 30 days before screening that included a long dwell of 8-16 hours using a solution containing 2.5% dextrose at a fill volume of 2-2.5L Number <ul style="list-style-type: none"> Efficacy study: treatment group (90); control group (85) Safety study: treatment group (175); control group (112) Mean age, range (years) <ul style="list-style-type: none"> Efficacy study: treatment group (54.4, 22 to 82); control group (55.2, 26 to 86) Safety study: treatment group (53.5, 22 to 83); control group (55.1, range 25 to 86) Sex (M/F) <ul style="list-style-type: none"> Efficacy study: treatment group (24/56); control group (26/59) Safety study: treatment group (93/82); control group (50/62) Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> PD solution containing 7.5% icodextrin with PD-2 electrolytes (Extraneal; Baxter) <p>Control group</p> <ul style="list-style-type: none"> 2.5% dextrose (2.5% Dianeal with PD-2 or PD-4 electrolytes) for the long dwell (dwell time, 8 to 16 hours). <p>Dialysate volume was either 2L or 2.5L, depending on the patient's usual prescriptions</p>
Outcomes	<p>Efficacy study</p> <ul style="list-style-type: none"> Net UF during the long overnight dwell in CAPD patients Also performed PET and calculated MTAC <p>Safety study</p> <ul style="list-style-type: none"> Death Change from baseline in membrane transport characteristics using the PET Incidence of adverse events Plasma levels of total icodextrin and metabolites, and clinically meaningful changes in laboratory parameters Chest radiographs Fluid imbalances Vital signs Physical examinations <p>During the study period, group added quality of life assessment as part of the study protocol</p>
Notes	<ul style="list-style-type: none"> Sponsored by Baxter

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer program
Allocation concealment (selection bias)	Low risk	Central list maintained by personnel not directly involved with the study

Wolfson 2002 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind status
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	High risk	High dropout rate: 118/287 (41%); efficacy (12/175, 6.9%); safety (118/287, 41%)
Selective reporting (reporting bias)	High risk	Limited clinical outcomes reported
Other bias	Unclear risk	Insufficient information to permit judgement

Yoo 2015

Methods	<ul style="list-style-type: none"> Study design: RCT Study duration: not reported Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> Country: Republic of Korea Setting: single centre Prevalent CAPD patients Number: treatment group (75); control group (39) Mean age $\pm$ SD (years): treatment group (50.9 $\pm$ 11.5); control group (50.7 $\pm$ 13.2) Sex (M/F): treatment group (34/41); control group (16/23) Exclusion criteria: not reported
Interventions	Treatment group <ul style="list-style-type: none"> Neutral pH, low GDP PD solution (Physioneal solution) Control group <ul style="list-style-type: none"> Conventional PD solution (Dianeal solution)
Outcomes	<ul style="list-style-type: none"> Biochemical maker (CA-125, IL-6) Peritoneal UF 4-hour dialysate:plasma creatinine Solute clearance Peritonitis rate
Notes	<ul style="list-style-type: none"> Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated random number

Yoo 2015 (Continued)

Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Open-label, unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	15.5% dropout
Selective reporting (reporting bias)	High risk	Limited outcomes are reported
Other bias	Unclear risk	Insufficient information to permit judgement

Zeier 2003

Methods	<ul style="list-style-type: none"> Study design: cross-over RCT Study duration: not reported Follow-up period: 16 weeks
Participants	<ul style="list-style-type: none"> Country: Germany Setting: multicentre Adult prevalent CAPD patients treated with exchange volumes of 1500 mL to 2500 mL Number: treatment group A (9); treatment group B (6) Mean age $\pm$ SD (years): treatment group A (49 ± 12); treatment group B (51 ± 8) Sex (M/F): treatment group A (3/6); treatment group B (5/1) Exclusion criteria: requirement of antibiotic treatment; history of peritonitis; seropositive for hepatitis B, C or HIV
Interventions	<ul style="list-style-type: none"> Group A <ul style="list-style-type: none"> Patients were either first exposed to PD fluid with neutral pH, low GDP PD solution (Gambrosol trio, Gambro Co) during eight weeks and subsequently switched to conventional PD fluid (Gambrosol, Gambro Co) for subsequently 8 weeks Group B <ul style="list-style-type: none"> Patients received reversal of treatment sequence
Outcomes	<ul style="list-style-type: none"> Determine the fate of GDP in PD fluids during PD by performing ex vivo studies from collected PD effluent after each treatment period CA125 concentrations from PD effluent
Notes	<ul style="list-style-type: none"> Author contacted to obtain clinical parameters, awaiting response

Risk of bias

Bias	Authors' judgement	Support for judgement
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Zeier 2003 (Continued)

Random sequence generation (selection bias)	Unclear risk	Insufficient information to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	High dropout rate, 6/21 (28.6%)
Selective reporting (reporting bias)	High risk	Limited reporting of clinical outcomes. However, the primary purpose of the study was to examine the non-clinical effects (e.g. biomarkers) of GDP in bio-compatible PD solutions
Other bias	Unclear risk	Insufficient information to permit judgement

APD - automated peritoneal dialysis; CAPD - continuous ambulatory peritoneal dialysis; CrCl - creatinine clearance; ESKD - end-stage kidney disease; GFR - glomerular filtration rate; HD - haemodialysis; HIV - human immunodeficiency virus; M/F - male/female; PET - peritoneal equilibration test; PD - peritoneal dialysis; RCT - randomised controlled trial; RRF - residual renal function; SD - standard deviation; SLE - systemic lupus erythromatosus; UF - ultrafiltration

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
BIOKID 2004	Wrong intervention: comparing two types of biocompatible PD solutions
Braide 2009	Wrong intervention: citrate supplementation rather than use of biocompatible PD fluids
Chang 2016	Wrong intervention: icodextrin versus non-icodextrin in the background of using low GDP biocompatible solutions
Chow 2014	Wrong intervention: icodextrin as part of treatment of peritonitis
Coester 2006	Wrong intervention: effect of glucose sparing therapy (NEP)
Dallas 2004	Wrong intervention: icodextrin versus Icodextrin/glucose combination novel fluid
de Fijter 1993	Study conducted over a short period with a view to assessing macrophage function hence study duration too short to evaluate pre-specified outcomes
EDEN 2013	Wrong intervention: glucose sparing therapy (NEP)
Fang 2008	Wrong intervention: neutral pH, low GDP PD solution as peritoneal equilibration test solution
Feriani 1993	Wrong intervention: two solutions with differences in buffers (bicarbonate against lactate)

Study	Reason for exclusion
Fischbach 2004	Study conducted over two days to examine the effect of PD solutions on intraperitoneal pressure. Duration of study was too short to evaluate pre-specified patient level clinical outcomes
Hiss 2013	Wrong intervention: normal versus reduced glucose content in the dialysis solution
Hwang 2006	Wrong intervention: icodextrin as peritoneal equilibration test solution
IMPENDIA 2013	Wrong intervention: glucose sparing therapy (NEP)
Jenkins 2003	Wrong intervention: icodextrin versus novel combination solution composed of icodextrin and dextrose
John 2008	Study conducted over one day to examine the effect of biocompatible PD solutions on baroreflex sensitivity. Duration of study was too short to evaluate pre-specified patient level clinical outcomes
le Poole 2004	Wrong intervention: amino acid-based dialysis solution
Liberek 2002	Study conducted following 2 overnight dwells (one week apart) of biocompatible and conventional PD solutions to measure inflammatory markers in the PD effluent. Duration of study was too short to evaluate pre-specified patient level clinical outcomes
Lui 2012	Wrong intervention: amino acid-containing dialysis solution
Martikainen 2005	Wrong intervention: amino acid-containing dialysis solution
Parikova 2007	Wrong intervention: neutral pH, low GDP PD solution as a peritoneal equilibration test solution
Pedersen 1985	Wrong intervention: comparing buffers in PD solution
Peers 1997	Wrong intervention: novel icodextrin/glucose combination fluid
Plum 1997	Wrong intervention: amino acid-containing dialysis solution
Rodriguez-Carmona 2007	Wrong intervention: amino acid-based dialysis solution
Sav 2009	Wrong intervention: twice-daily icodextrin versus daily icodextrin
Sav 2010	Wrong intervention: twice-daily icodextrin versus daily icodextrin
Selby 2005	Study conducted over two days to examine the effect of PD solutions on haemodynamic parameters. Duration of study was too short to evaluate pre-specified patient level clinical outcomes
Selby 2007a	Wrong intervention: amino acid fluid
Smit 2000	Wrong intervention: glycerol-based fluid
Smit 2001	Wrong intervention: different strengths of glucose solutions
Ueda 2000	Wrong intervention: amino acid fluid study
Van Biesen 2004	Wrong intervention: amino acid fluid study
Yehia 2014	Wrong intervention: icodextrin versus exchange-free dialysis regimen in the setting of peritonitis

Study	Reason for exclusion
Yoon 2014	Wrong intervention: icodextrin versus non -icodextrin in the background of using biocompatible solution (physioneal)

GDP - glucose degradation products; NEP - neutral endopeptidase; PD - peritoneal dialysis

Characteristics of studies awaiting assessment *[ordered by study ID]*

Cho 2010

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Randomisation method: not reported Blinding: not reported Intention to treat: unclear Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> Country: Republic of Korea Setting: single centre Incident adult CAPD patients
Interventions	<p>Group 1</p> <ul style="list-style-type: none"> 55 participants Neutral pH, low GDP PD solution (Balance, Fresenius Medical Care, Germany) <p>Group 2</p> <ul style="list-style-type: none"> 23 participants Conventional PD solution (StaySafe, Fresenius Medical Care, Germany) <p>Group 3</p> <ul style="list-style-type: none"> 22 participants Neutral pH, low GDP PD solution (Physioneal, Baxter Healthcare, USA) <p>Group 4</p> <ul style="list-style-type: none"> 26 participants Conventional PD solution (Dianeal, Baxter Healthcare, USA)
Outcomes	<ul style="list-style-type: none"> UF volume Glucose absorption 24-hour peritoneal UF Urine volume Body weight Bioimpedance analysis for fluid status assessment
Notes	<ul style="list-style-type: none"> Abstract format only. Unable to obtain additional information from authors

Dai 2010

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Randomisation method: not reported Blinding: double blind
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Dai 2010 (Continued)

	<ul style="list-style-type: none"> • Intention to treat: unclear • Follow-up period: 4 weeks
Participants	<ul style="list-style-type: none"> • Country: China • Setting: single centre • CAPD patients
Interventions	<ul style="list-style-type: none"> • 7.5% icodextrin (27) or glucose (27) at night for 4 weeks
Outcomes	<ul style="list-style-type: none"> • 4-hour dialysate:plasma creatinine • UF volume • CrCl
Notes	<ul style="list-style-type: none"> • Unable to access full-text

De Los Rios 2016

Methods	<ul style="list-style-type: none"> • Study design: cross-over RCT • Randomisation method: not reported • Blinding: open label • Intention to treat: yes • Follow-up period: 16 weeks
Participants	<ul style="list-style-type: none"> • Country: Spain • Setting: multicentre • Prevalent adult APD patients
Interventions	<ul style="list-style-type: none"> • neutral pH, low GDP dextrosed based solution (balance)
Outcomes	<ul style="list-style-type: none"> • peritonitis • peritoneal UF • urine volume
Notes	<ul style="list-style-type: none"> • Unable to obtain data from the first phase of the cross-over study

Do 2006a

Methods	<ul style="list-style-type: none"> • Study design: RCT • Randomisation method: not reported • Blinding: not reported • Intention to treat: not reported • Follow-up period: uncertain
Participants	<ul style="list-style-type: none"> • Country: Republic of Korea • Setting: single centre • Incident CAPD patients who survived more than 3 months
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • StaySafe Balance (Fresenius Medical Care, Germany) or Physioneal (Baxter, USA)

Do 2006a (Continued)

	Control group
	<ul style="list-style-type: none"> StaySafe (Fresenius Medical Care, Germany) or Dianeal (Baxter, USA)
Outcomes	<ul style="list-style-type: none"> high sensitive CRP CA-125 of dialysate peritoneal equilibrium test patients survival
Notes	<ul style="list-style-type: none"> Information available only in abstract form; unable to obtain further data

Infante 2000

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Randomisation method: not reported Blinding: not reported Intention to treat: unclear Follow-up period: 12 months
Participants	<ul style="list-style-type: none"> Country: Italy Setting: single centre, university hospital Prevalent adult PD patients (24)
Interventions	Treatment group <ul style="list-style-type: none"> Bicarbonate-buffered PD solution Control group <ul style="list-style-type: none"> Lactate-buffered PD solution
Outcomes	<ul style="list-style-type: none"> Mesothelial biomarkers (e.g. CA125)
Notes	<ul style="list-style-type: none"> Information available only in abstract form; clinical outcomes of interest not available

Kim 2006

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Study duration: not reported Duration of follow-up: 12 months
Participants	<ul style="list-style-type: none"> Country: South Korea Setting: single centre Well dialysed CAPD patients Number: treatment group (26); control group (27) Mean age $\pm$ SD (years): not reported Sex (M/F): not reported Exclusion criteria: not reported
Interventions	Treatment group <ul style="list-style-type: none"> 25 mmol/L bicarbonate/15 mmol/L lactate PD solution

Kim 2006 (Continued)

	Control group
	<ul style="list-style-type: none"> 40 mmol/L lactate solution
Outcomes	<ul style="list-style-type: none"> Mean pH Plasma bicarbonate UF BP Dialysis adequacy peritoneal permeability Anaemia Peritonitis rate
Notes	<ul style="list-style-type: none"> Abstract-only publication; no data available for analysis

Kocyigit 2015

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Randomisation method: sealed enveloped Blinding: not reported for participants, investigators and outcome assessors Intention to treat: no Follow-up period: 12 months Loss to follow-up: 8%
Participants	<ul style="list-style-type: none"> Country: Turkey Setting: multicentre Incident adult PD patients Exclusion criteria: major cardiovascular disease (history of acute coronary syndrome or coronary artery bypass surgery); cardiomyopathy and cardiac arrhythmia; peripheral artery disease
Interventions	<ul style="list-style-type: none"> Physioneal solution for 12 months
Outcomes	<ul style="list-style-type: none"> BP ECG
Notes	<ul style="list-style-type: none"> Unable to obtain data for outcomes of interest including RRF, UF, urine volume, peritonitis

NCT01753154

Methods	<ul style="list-style-type: none"> Study design: cross-over RCT Randomisation method: not reported Blinding: open label Intention to treat: unclear Follow-up period: 16 weeks
Participants	<ul style="list-style-type: none"> Countries: Poland and Spain Setting: multicentre prevalent APD patients
Interventions	<ul style="list-style-type: none"> Balance PD solution for 8 weeks then conventional PD solution for another 8 weeks

NCT01753154 (Continued)

Outcomes	<ul style="list-style-type: none"> • RRF • Peritoneal UF • Peritoneal solute clearance • fluid status
Notes	<ul style="list-style-type: none"> • Study recently completed; no data available

Opatrna 2002

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT • Randomisation method: unclear • Blinding: not reported for participants, investigators and outcome assessors • Intention to treat: yes • Follow-up period: 3 months • Loss to follow-up: unclear
Participants	<ul style="list-style-type: none"> • Country: Czech Republic • Setting: single centre • CAPD-treated patients with difficult hydration control versus a control group
Interventions	<ul style="list-style-type: none"> • Icodextrin for the night-time exchange for a period of 3 months
Outcomes	<ul style="list-style-type: none"> • UF • BP
Notes	<ul style="list-style-type: none"> • No data given in the abstract for the control group

Rodriguez-Carmona 2012

Methods	<ul style="list-style-type: none"> • Study design: cross-over design • Randomisation method: not reported • Blinding: open label • Intention to treat: unclear • Follow-up period: 10 weeks
Participants	<ul style="list-style-type: none"> • Country: Spain • Setting: single centre • Prevalent PD patients • Exclusion criteria: age < 18 or > 85 years; PD for < 2 months; significant clinical events (including peritonitis) during the previous 3 months; unwillingness or inability to cooperate
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Neutral pH, low GDP PD solution (Physioneal Clear Flex, Baxter) <p>Control group</p> <ul style="list-style-type: none"> • Conventional PD solution (Dianeal, Baxter) <p>5 weeks in each arm then cross-over</p>
Outcomes	<ul style="list-style-type: none"> • Body weight

Biocompatible dialysis fluids for peritoneal dialysis (Review)

Rodriguez-Carmona 2012 *(Continued)*

	<ul style="list-style-type: none"> • Urine output • RRF • Peritoneal small solute clearance • Peritoneal UF • 4-hour dialysate:plasma creatinine
Notes	<ul style="list-style-type: none"> • Unable to obtain data from the first phase of cross-over study

Yang 2002b

Methods	<ul style="list-style-type: none"> • Study design: cross-over RCT • Randomisation method: not reported • Blinding: open label • Intention to treat: unclear • Follow-up period: 8 weeks
Participants	<ul style="list-style-type: none"> • Countries: Taiwan • Setting: single centre • Prevalent CAPD patients
Interventions	<ul style="list-style-type: none"> • Received either 7.5% icodextrin or 2.5% dextrose for the overnight dwell for 28 days and then cross-over for another 28 days
Outcomes	<ul style="list-style-type: none"> • UF • 4-hour dialysate:plasma creatinine • BP
Notes	<ul style="list-style-type: none"> • Unable to obtain data from the first phase of cross-over study

APD - automated peritoneal dialysis; BP - blood pressure; CAPD - continuous ambulatory peritoneal dialysis; CrCl - creatinine clearance; CRP - C-reactive protein; GDP - glucose degradation products; ECG - echocardiogram; PD - peritoneal dialysis; RCT - randomised controlled trial; RRF - residual renal function; UF - ultrafiltration

Characteristics of ongoing studies *[ordered by study ID]*
NCT01228279

Trial name or title	Sympathetic Activity in Patients With End-stage Renal Disease on Peritoneal Dialysis (SAPD)
Methods	<ul style="list-style-type: none"> • Study design: parallel • Randomisation method: not reported • Blinding: open label, single blind (outcome assessor) • Intention to treat: unclear • Follow-up period: 18 weeks
Participants	<ul style="list-style-type: none"> • Countries: Canada • Setting: single centre • Incident CAPD and CCPD patients
Interventions	<ul style="list-style-type: none"> • Icodextrin for the night-time exchange for a period of 12 weeks (7 to 18 week of study)
Outcomes	<ul style="list-style-type: none"> • muscle sympathetic nerve activity

Biocompatible dialysis fluids for peritoneal dialysis (Review)

NCT01228279 (Continued)

- change in extracellular volume
- BP
- RRF

Starting date	• July 2017
Contact information	Marcel Ruzicka, MD, mruzicka@ottawahospital.on.ca
Notes	

BP - blood pressure; CAPD - continuous ambulatory peritoneal dialysis; CCPD - continuous cycling peritoneal dialysis; RRF - residual renal function

DATA AND ANALYSES

Comparison 1. Low GDP (all buffer types) versus standard glucose dialysate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Residual renal function	15	835	Std. Mean Difference (IV, Random, 95% CI)	0.19 [0.05, 0.33]
1.1 3 months	3	143	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.37, 0.29]
1.2 12 months	6	349	Std. Mean Difference (IV, Random, 95% CI)	0.18 [-0.04, 0.39]
1.3 24 months	5	218	Std. Mean Difference (IV, Random, 95% CI)	0.33 [0.06, 0.60]
1.4 3 years +	1	125	Std. Mean Difference (IV, Random, 95% CI)	0.24 [-0.11, 0.59]
2 Residual renal function: up to 12 months	12	860	Std. Mean Difference (IV, Random, 95% CI)	0.18 [0.05, 0.32]
2.1 4 weeks	1	48	Std. Mean Difference (IV, Random, 95% CI)	0.11 [-0.46, 0.67]
2.2 3 months	3	143	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.37, 0.29]
2.3 6 months	6	440	Std. Mean Difference (IV, Random, 95% CI)	0.32 [0.10, 0.54]
2.4 8 months	1	91	Std. Mean Difference (IV, Random, 95% CI)	-0.03 [-0.44, 0.38]
2.5 9 months	1	138	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.12, 0.55]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Residual renal function: 12 months up to 24 months	10	641	Std. Mean Difference (IV, Random, 95% CI)	0.25 [0.10, 0.41]
3.1 12 months	8	545	Std. Mean Difference (IV, Random, 95% CI)	0.26 [0.09, 0.43]
3.2 18 months	2	96	Std. Mean Difference (IV, Random, 95% CI)	0.23 [-0.17, 0.64]
4 Residual renal function: 24 months and beyond	6	343	Std. Mean Difference (IV, Random, 95% CI)	0.30 [0.08, 0.51]
4.1 24 months	5	218	Std. Mean Difference (IV, Random, 95% CI)	0.33 [0.06, 0.60]
4.2 3 years +	1	125	Std. Mean Difference (IV, Random, 95% CI)	0.24 [-0.11, 0.59]
5 Residual renal function: PD fluid types	15	835	Std. Mean Difference (IV, Random, 95% CI)	0.19 [0.05, 0.33]
5.1 Balance	9	495	Std. Mean Difference (IV, Random, 95% CI)	0.20 [0.02, 0.37]
5.2 Purely bicarbonate buffered	3	58	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.46, 0.59]
5.3 Multiple fluid types in treatment group	2	218	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.20, 0.41]
5.4 Gambrosol trio	1	64	Std. Mean Difference (IV, Random, 95% CI)	0.52 [0.02, 1.02]
6 Urine volume	11	791	Mean Difference (IV, Random, 95% CI)	114.37 [47.09, 181.65]
6.1 3 months	2	120	Mean Difference (IV, Random, 95% CI)	-0.54 [-515.46, 514.38]
6.2 12 months	6	392	Mean Difference (IV, Random, 95% CI)	120.94 [45.49, 196.39]
6.3 24 months	2	154	Mean Difference (IV, Random, 95% CI)	123.27 [-51.83, 298.36]
6.4 3 years +	1	125	Mean Difference (IV, Random, 95% CI)	270.6 [10.53, 530.67]
7 Urine volume: up to 12 months	10	819	Mean Difference (IV, Random, 95% CI)	69.72 [-55.95, 195.40]
7.1 1 month	1	50	Mean Difference (IV, Random, 95% CI)	-30.0 [-399.49, 339.49]
7.2 3 months	2	120	Mean Difference (IV, Random, 95% CI)	-0.54 [-515.46, 514.38]
7.3 6 months	6	558	Mean Difference (IV, Random, 95% CI)	157.25 [58.48, 256.01]
7.4 8 months	1	91	Mean Difference (IV, Random, 95% CI)	-147.2 [-262.68, -31.72]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8 Urine volume: 12 months up to 24 months	8	579	Mean Difference (IV, Random, 95% CI)	110.57 [40.81, 180.34]
8.1 12 months	6	392	Mean Difference (IV, Random, 95% CI)	120.94 [45.49, 196.39]
8.2 18 months	2	187	Mean Difference (IV, Random, 95% CI)	60.94 [-186.22, 308.10]
9 Urine volume: 24 months and beyond	3	279	Mean Difference (IV, Random, 95% CI)	169.22 [23.98, 314.46]
9.1 24 months	2	154	Mean Difference (IV, Random, 95% CI)	123.27 [-51.83, 298.36]
9.2 3 years +	1	125	Mean Difference (IV, Random, 95% CI)	270.6 [10.53, 530.67]
10 Urine volume: PD fluid types	11	791	Mean Difference (IV, Random, 95% CI)	114.37 [47.09, 181.65]
10.1 Balance	7	482	Mean Difference (IV, Random, 95% CI)	120.48 [47.99, 192.97]
10.2 Purely bicarbonate buffered	1	27	Mean Difference (IV, Random, 95% CI)	345.50 [-274.17, 965.17]
10.3 Multiple fluid types in the treatment group	2	218	Mean Difference (IV, Random, 95% CI)	37.84 [-423.31, 498.99]
10.4 Gambrosol trio	1	64	Mean Difference (IV, Random, 95% CI)	130.0 [-105.87, 365.87]
11 Anuria	2	246	Risk Ratio (M-H, Random, 95% CI)	0.56 [0.18, 1.75]
12 Peritoneal ultrafiltration: 4 hours	9	414	Std. Mean Difference (IV, Random, 95% CI)	-0.42 [-0.74, -0.10]
12.1 2.26%/2.5% glucose	4	218	Std. Mean Difference (IV, Random, 95% CI)	-0.35 [-0.76, 0.07]
12.2 3.86%/4.25% glucose	5	196	Std. Mean Difference (IV, Random, 95% CI)	-0.49 [-1.08, 0.11]
13 4-hour dialysate:plasma creatinine (2.27%, 2.4%, or 2.5% glucose)	10	746	Mean Difference (IV, Random, 95% CI)	0.01 [0.00, 0.03]
13.1 3 months	1	24	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.11, 0.09]
13.2 12 months	6	448	Mean Difference (IV, Random, 95% CI)	0.01 [-0.01, 0.03]
13.3 24 months	2	149	Mean Difference (IV, Random, 95% CI)	0.01 [-0.01, 0.04]
13.4 3 years +	1	125	Mean Difference (IV, Random, 95% CI)	0.06 [0.02, 0.10]
14 4-hour dialysis:plasma creatinine (patient characteristics)	10	746	Mean Difference (IV, Random, 95% CI)	0.01 [0.00, 0.03]
14.1 Incident patients	7	554	Mean Difference (IV, Random, 95% CI)	0.02 [-0.00, 0.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.2 Prevalent patients	3	192	Mean Difference (IV, Random, 95% CI)	0.00 [-0.03, 0.04]
15 4-hour dialysis:plasma creatinine (PD fluid types)	10	746	Mean Difference (IV, Random, 95% CI)	0.01 [0.00, 0.03]
15.1 Balance	6	470	Mean Difference (IV, Random, 95% CI)	0.01 [-0.01, 0.03]
15.2 Purely bicarbonate buffered	1	24	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.11, 0.09]
15.3 multiple fluid type in the treatment group	2	187	Mean Difference (IV, Random, 95% CI)	0.03 [-0.04, 0.10]
15.4 Gambrosol trio	1	65	Mean Difference (IV, Random, 95% CI)	0.02 [-0.01, 0.05]
16 4-hour dialysis:plasma creatinine (study design)	10	746	Mean Difference (IV, Random, 95% CI)	0.01 [0.00, 0.03]
16.1 Single centre	4	277	Mean Difference (IV, Random, 95% CI)	0.01 [-0.01, 0.04]
16.2 Multicentre	6	469	Mean Difference (IV, Random, 95% CI)	0.02 [-0.00, 0.04]
17 Peritoneal creatinine clearance [L/wk/1.73 m ²]	7	510	Mean Difference (IV, Random, 95% CI)	-0.44 [-2.03, 1.15]
17.1 3 months	1	24	Mean Difference (IV, Random, 95% CI)	-7.46 [-20.65, 5.73]
17.2 12 months	4	273	Mean Difference (IV, Random, 95% CI)	-0.31 [-2.28, 1.66]
17.3 24 months	1	88	Mean Difference (IV, Random, 95% CI)	-2.60 [-6.80, 1.60]
17.4 3 years +	1	125	Mean Difference (IV, Random, 95% CI)	1.30 [-2.37, 4.97]
18 Peritoneal Kt/V urea	6	422	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.12, 0.09]
18.1 3 months	1	24	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.78, 0.76]
18.2 12 months	4	273	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.18, 0.16]
18.3 3 years +	1	125	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.18, 0.10]
19 Incidence of peritonitis	12	1055	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.92, 1.72]
19.1 8 weeks follow-up	1	59	Risk Ratio (M-H, Random, 95% CI)	1.58 [0.49, 5.10]
19.2 24 weeks	1	73	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.58, 2.36]
19.3 12 months follow-up	5	507	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.93, 1.73]
19.4 18 months follow-up	1	69	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.56, 2.07]
19.5 24 months follow-up	4	347	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.62, 2.84]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20 Peritonitis rate (episodes/total patient-months)	10	18184	Risk Ratio (M-H, Random, 95% CI)	1.18 [0.84, 1.64]
21 Incidence of peritonitis: attrition bias risk	12	1055	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.92, 1.72]
21.1 Low risk	3	359	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.47, 0.90]
21.2 High risk	9	696	Risk Ratio (M-H, Random, 95% CI)	1.58 [1.28, 1.96]
22 Inflow pain	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
22.1 6 months	1	58	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.24, 1.08]
23 Hospitalisation	2	230	Mean Difference (IV, Random, 95% CI)	3.02 [-7.08, 13.12]
23.1 12 months	1	48	Mean Difference (IV, Random, 95% CI)	-0.40 [-6.71, 5.91]
23.2 24 months	1	182	Mean Difference (IV, Random, 95% CI)	10.79 [-4.28, 25.86]
24 Technique failure (death-censored)	15	1275	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.75, 1.63]
24.1 3 months	2	52	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
24.2 6 months	2	179	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.04, 2.97]
24.3 12 months	5	478	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.31, 2.21]
24.4 24 months	5	441	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.70, 1.90]
24.5 3 years +	1	125	Risk Ratio (M-H, Random, 95% CI)	2.89 [0.58, 14.33]
25 Death (all causes)	15	1229	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.47, 1.14]
25.1 3 months	2	52	Risk Ratio (M-H, Random, 95% CI)	0.16 [0.01, 3.09]
25.2 12 months follow-up	7	633	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.29, 1.19]
25.3 18 months follow-up	1	69	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.02, 1.84]
25.4 24 months follow-up	4	350	Risk Ratio (M-H, Random, 95% CI)	1.18 [0.56, 2.51]
25.5 3 years +	1	125	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.29, 2.03]

Analysis 1.1. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 1 Residual renal function.

Analysis 1.2. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 2 Residual renal function: up to 12 months.

Analysis 1.3. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 3 Residual renal function: 12 months up to 24 months. **Analysis 1.4. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 4 Residual renal function: 24 months and beyond.**

Analysis 1.5. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 5 Residual renal function: PD fluid types.

Analysis 1.6. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 6 Urine volume.

Analysis 1.7. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 7 Urine volume: up to 12 months.

Analysis 1.8. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 8 Urine volume: 12 months up to 24 months.

Analysis 1.9. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 9 Urine volume: 24 months and beyond.

Study or subgroup	Neutral pH, low GDP		Standard glucose		Mean Difference	Weight	Mean Difference			
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI			
Test for overall effect: Z=2.28(P=0.02)										
Test for subgroup differences: Chi²=0.85, df=1 (P=0.36), I²=0%										
					-1000	-500	0	500	1000	
					Favours standard glucose			Favours low GDP		

Analysis 1.10. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 10 Urine volume: PD fluid types.

Study or subgroup	Neutral pH, low GDP		Standard glucose		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
1.10.1 Balance							
Szeto 2015	25	810 (660)	28	580 (520)		4.29%	230[-92.54,552.54]
Szeto 2007	24	800 (600)	24	690 (520)		4.42%	110[-207.65,427.65]
BALNET 2008	36	750 (679)	33	532 (408)		6.46%	218[-43.87,479.87]
balANZ 2010	42	814 (624)	48	699 (639)		6.48%	115[-146.33,376.33]
Cho 2013	32	624.7 (487.7)	28	681.8 (460.1)		7.65%	-57.1[-297.09,182.89]
Park 2012a	56	714 (537)	38	644 (575)		8.27%	70[-160.66,300.66]
Choi 2008	38	280 (236.6)	30	143 (172.9)		41.02%	137[39.6,234.4]
Subtotal ***	253		229			78.59%	120.48[47.99,192.97]
Heterogeneity: Tau²=0; Chi²=3.38, df=6(P=0.76); I²=0%							
Test for overall effect: Z=3.26(P=0)							
1.10.2 Purely bicarbonate buffered							
Weiss 2009	15	1346.1 (870.8)	12	1000.6 (770)		1.17%	345.5[-274.17,965.17]
Subtotal ***	15		12			1.17%	345.5[-274.17,965.17]
Heterogeneity: Not applicable							
Test for overall effect: Z=1.09(P=0.27)							
1.10.3 Multiple fluid types in the treatment group							
Fan 2008	44	800 (663.3)	49	1000 (700)		5.78%	-200[-477.18,77.18]
Lai 2012a	58	745.7 (819.2)	67	475.1 (635.9)		6.54%	270.6[10.53,530.67]
Subtotal ***	102		116			12.32%	37.84[-423.31,498.99]
Heterogeneity: Tau²=91929.02; Chi²=5.89, df=1(P=0.02); I²=83.02%							
Test for overall effect: Z=0.16(P=0.87)							
1.10.4 Gambrosol trio							
TRIO 2016	30	889 (501)	34	759 (456)		7.92%	130[-105.87,365.87]
Subtotal ***	30		34			7.92%	130[-105.87,365.87]
Heterogeneity: Not applicable							
Test for overall effect: Z=1.08(P=0.28)							
Total ***	400		391			100%	114.37[47.09,181.65]
Heterogeneity: Tau²=403.08; Chi²=10.28, df=10(P=0.42); I²=2.77%							
Test for overall effect: Z=3.33(P=0)							
Test for subgroup differences: Chi²=0.63, df=1 (P=0.89), I²=0%							
					-1000 -500 0 500 1000		
					Favours standard glucose Favours low GDP		

Analysis 1.11. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 11 Anuria.

Analysis 1.12. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 12 Peritoneal ultrafiltration: 4 hours.

Analysis 1.13. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 13 4-hour dialysate:plasma creatinine (2.27%, 2.4%, or 2.5% glucose).

Analysis 1.14. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 14 4-hour dialysis:plasma creatinine (patient characteristics).

Analysis 1.15. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 15 4-hour dialysis:plasma creatinine (PD fluid types).

Analysis 1.16. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 16 4-hour dialysis:plasma creatinine (study design).

Analysis 1.17. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 17 Peritoneal creatinine clearance [L/wk/1.73 m²].

Analysis 1.18. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 18 Peritoneal Kt/V urea.

Analysis 1.19. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 19 Incidence of peritonitis.

Analysis 1.20. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 20 Peritonitis rate (episodes/total patient-months).

Analysis 1.21. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 21 Incidence of peritonitis: attrition bias risk.

Analysis 1.22. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 22 Inflow pain.

Analysis 1.23. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 23 Hospitalisation.

Analysis 1.24. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 24 Technique failure (death-censored).

Analysis 1.25. Comparison 1 Low GDP (all buffer types) versus standard glucose dialysate, Outcome 25 Death (all causes).

Comparison 2. Glucose polymer (icodextrin) versus standard glucose dialysate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Daily ultrafiltration	4	102	Mean Difference (IV, Random, 95% CI)	448.54 [289.28, 607.80]
1.1 3 months	1	33	Mean Difference (IV, Random, 95% CI)	416.0 [236.26, 595.74]
1.2 4 months	1	32	Mean Difference (IV, Random, 95% CI)	607.0 [-2164.12, 3378.12]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3 24 months	2	37	Mean Difference (IV, Random, 95% CI)	510.55 [10.10, 1011.00]
2 Uncontrolled fluid overload	2	100	Risk Ratio (M-H, Random, 95% CI)	0.30 [0.15, 0.59]
2.1 24 months	1	41	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.10, 1.01]
2.2 12 months	1	59	Risk Ratio (M-H, Random, 95% CI)	0.28 [0.12, 0.67]
3 Residual renal function	4	114	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.26, 0.49]
3.1 Residual GFR (mL/min)	1	32	Std. Mean Difference (IV, Random, 95% CI)	-0.05 [-0.75, 0.66]
3.2 Renal CrCl (mL/min/1.73 m ²)	1	25	Std. Mean Difference (IV, Random, 95% CI)	0.28 [-0.51, 1.07]
3.3 Renal CrCl (mL/min)	1	24	Std. Mean Difference (IV, Random, 95% CI)	-0.23 [-1.05, 0.58]
3.4 Residual renal function (mL/min/1.73 m ²)	1	33	Std. Mean Difference (IV, Random, 95% CI)	0.40 [-0.29, 1.09]
4 Urine volume	3	69	Mean Difference (IV, Random, 95% CI)	-88.88 [-356.88, 179.12]
4.1 4 months	1	32	Mean Difference (IV, Random, 95% CI)	-35.0 [-2561.49, 2491.49]
4.2 2 years	2	37	Mean Difference (IV, Random, 95% CI)	-89.49 [-359.01, 180.03]
5 Change in urine volume (mL)			Other data	No numeric data
6 Peritoneal creatinine clearance	3	237	Std. Mean Difference (IV, Random, 95% CI)	0.36 [-0.24, 0.96]
6.1 4 weeks	1	183	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.22, 0.36]
6.2 3 months	1	33	Std. Mean Difference (IV, Random, 95% CI)	1.03 [0.30, 1.77]
6.3 12 months	1	21	Std. Mean Difference (IV, Random, 95% CI)	0.11 [-0.74, 0.97]
7 Episodes of peritonitis	6	667	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.77, 1.18]
7.1 4 weeks	1	201	Risk Ratio (M-H, Random, 95% CI)	5.25 [0.26, 108.05]
7.2 6 weeks follow-up	1	22	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 3 months	1	60	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.12, 5.43]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.4 12 months follow-up	2	346	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.69, 1.58]
7.5 2 years follow-up	1	38	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.63, 1.22]
8 Rash	3	755	Risk Ratio (M-H, Random, 95% CI)	2.51 [0.59, 10.72]
9 Technique failure (death-censored)	4	350	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.32, 1.12]
10 Death (all causes)	6	816	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.32, 2.13]
10.1 4 weeks follow-up	1	201	Risk Ratio (M-H, Random, 95% CI)	3.15 [0.13, 76.45]
10.2 6 months follow-up	2	249	Risk Ratio (M-H, Random, 95% CI)	0.19 [0.01, 4.00]
10.3 12 months	1	287	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.34, 3.74]
10.4 2 years follow-up	2	79	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.04, 3.00]

Analysis 2.1. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 1 Daily ultrafiltration.

Analysis 2.2. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 2 Uncontrolled fluid overload.

Analysis 2.3. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 3 Residual renal function.

Analysis 2.4. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 4 Urine volume.

Analysis 2.5. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 5 Change in urine volume (mL).

Study	Time point	Change in urine volume (mL)	
		Glucose polymer	Standard glucose solution
Davies 2003	1 month	-44.3	-44.1
Davies 2003	3 months	-34.6	-56.6
Davies 2003	6 months	-10.7	-126.6

Analysis 2.6. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 6 Peritoneal creatinine clearance.

Analysis 2.7. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 7 Episodes of peritonitis.

Analysis 2.8. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 8 Rash.

Analysis 2.9. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 9 Technique failure (death-censored).

Analysis 2.10. Comparison 2 Glucose polymer (icodextrin) versus standard glucose dialysate, Outcome 10 Death (all causes).

ADDITIONAL TABLES

Table 1. Summary of analyses

Outcome	Subgroup analyses performed	'Other data' tables
Neutral pH, low GDP PD solutions versus conventional PD solutions		
Residual renal function	<ul style="list-style-type: none"> Study duration Incident versus prevalent patients Single versus multicentre study Parallel versus cross-over design PD fluid types Presence of selection bias Presence of other significant bias Weekly residual GFR in patients with baseline GFR > 2 mL/ min/ 1.73 m² 	--
Urine volume	<ul style="list-style-type: none"> Study duration Standard versus hypertonic PET Single versus multicentre study Parallel versus cross-over design Presence of selection bias Presence of other significant bias 	--
Anuria	--	--
4-hour peritoneal ultrafiltration	<ul style="list-style-type: none"> Study duration Standard versus hypertonic PET Single versus multicentre study Parallel versus cross-over design Presence of selection bias Presence of other significant bias 	--
Daily peritoneal ultrafiltration	<ul style="list-style-type: none"> Study duration Incident versus prevalent patients Single versus multicentre study Parallel versus cross-over design Presence of selection bias Presence of other significant bias 	--

Table 1. Summary of analyses (Continued)

Peritoneal solute transport rate (4-hour dialysate:plasma creatinine)	<ul style="list-style-type: none"> • Study duration • Presence of selection bias • Presence of other significant bias 	--
Dialysis adequacy (CrCl/ Kt/V urea)	--	Dialysis adequacy and peritoneal transport in anuric patients (median (IQR))
Inflow pain	--	--
Peritonitis	<ul style="list-style-type: none"> • Presence of selection bias • Presence of attrition bias • Presence of other significant bias 	--
Technique failure	--	--
Hospitalisation	--	--
Death (all causes)	--	--
Glucose polymer (icodextrin) versus conventional PD solution		
Uncontrolled fluid overload	--	--
Rash	--	--
Residual renal function	--	--
Urine volume	--	Change in urine volume (mL)
Daily peritoneal ultrafiltration	Change in ultrafiltration volume/membrane transport characteristics	--
Peritoneal solute transport rate (4-hour dialysate:plasma creatinine)	--	--
Dialysis adequacy (CrCl)	Change in peritoneal CrCl/membrane transport characteristics	--
Peritonitis	--	--
Technique failure	--	--
Death (all causes)	--	--

CrCl - creatinine clearance; GFR - glomerular filtration rate; IQR - interquartile range; PET - peritoneal equilibration test; PD - peritoneal dialysis

Table 2. Adverse effects reported in studies

Adverse events	Standard glucose solution		Low GDP solution		Studies reporting outcome
	No. events	No. at risk	No. events	No. at risk	

Table 2. Adverse effects reported in studies (Continued)

Neutral pH, low GDP PD solution (excluding peritonitis, death)

Exit site infection	6	91	4	91	balANZ 2010
	0	19	5	40	Coles 1997
	1	36	3	37	Feriani 1998
Tunnel infection	2	91	1	91	balANZ 2010
Non-PD related infection/general infection	20	91	4	91	balANZ 2010
	0	19	6	40	Coles 1997
Inadequate dialysis	1	91	1	91	balANZ 2010
Fluid overload/hypervolaemia	3	91	1	91	balANZ 2010
	1	19	4	40	Coles 1997
	2	36	0	37	Feriani 1998
Hypertension	2	19	3	40	Coles 1997
	1	36	0	37	Feriani 1998
Hypotension	0	36	1	37	Feriani 1998
Hernia	11	91	10	91	balANZ 2010
	1	36	0	37	Feriani 1998
Peritoneal leak	3	91	1	91	balANZ 2010
Catheter blockage	4	91	5	91	balANZ 2010
Malposition	2	91	1	91	balANZ 2010
Gastrointestinal disorder	6	91	14	91	balANZ 2010
Abdominal pain	0	19	3	40	Coles 1997
Pancreatitis	1	36	0	37	Feriani 1998
Enteritis	0	36	2	37	Feriani 1998
Vomiting	0	36	1	37	Feriani 1998
Newly diagnosed cancer	3	91	4	91	balANZ 2010
Arthritis	1	36	0	37	Feriani 1998
Angina	0	36	1	37	Feriani 1998
Apoplexy	1	36	1	37	Feriani 1998
Hypercalcaemia	0	19	3	40	Coles 1997

Table 2. Adverse effects reported in studies *(Continued)*

	3	36	2	37	Feriani 1998
Hypocalcaemia	0	19	3	40	Coles 1997
Hyperphosphataemia	3	19	4	40	Coles 1997
Hyperglycaemia	1	36	0	37	Feriani 1998
Glucose polymer (icodextrin) (excluding rash, peritonitis, death)					
Abdominal discomfort	1	103	0	98	Lin 2009a
Anaemia	24	29	6	30	Paniagua 2008
	26	112	39	175	Wolfson 2002
Arterial emboli	1	103	0	106	MIDAS 1994
Cardiac failure	1	103	1	106	MIDAS 1994
Cerebrovascular accident	0	103	2	106	MIDAS 1994
Diabetic foot	5	29	1	30	Paniagua 2008
Dizzy	0	103	1	98	Lin 2009a
Electrolyte disturbances	4	29	1	30	Paniagua 2008
Exit site infection	3	27	4	33	STARCH 2015
	24	112	28	175	Wolfson 2002
Fatigue	0	103	2	98	Lin 2009a
Fluid overload	17	132	6	136	Lin 2009a
	17	29	5	30	Paniagua 2008
Headache	9	112	25	175	Wolfson 2002
Stroke	1	27	0	33	STARCH 2015
Hyperglycaemia	27	29	8	30	Paniagua 2008
Hypotension	28	215	25	273	Lin 2009a
					Wolfson 2002
Myocardial infarction	4	103	2	106	MIDAS 1994
	3	29	0	30	Paniagua 2008
Pain	18	112	30	175	Wolfson 2002
Pleural effusion	6	29	1	30	Paniagua 2008
Pneumonia	0	103	1	106	MIDAS 1994

Table 2. Adverse effects reported in studies (Continued)

Pulmonary embolism	0	103	1	106	MIDAS 1994
Thirsty	0	103	1	98	Lin 2009a
Uncontrolled hypertension	0	103	1	106	MIDAS 1994
	21	112	40	175	Wolfson 2002
Hypotension	1	27	3	33	STARCH 2015
Hypertension	0	27	1	33	STARCH 2015
Congestion	1	27	0	33	STARCH 2015
Upper respiratory tract infection	25	112	41	175	Wolfson 2002
Vomiting	1	103	0	98	Lin 2009a

GDP - glucose degradation products; PD - peritoneal dialysis

APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	<ol style="list-style-type: none"> peritoneal dialysis:ti,ab,kw (CAPD or CCPD or APD or PD):ti,ab,kw (#1 OR #2) biocompatib*:ti,ab,kw dialysis solution*.ti,ab,kw bicarbonate*:ti,ab,kw (lactate* or lactic next acid*):ti,ab,kw buffer*:ti,ab,kw (ph next neutral):ti,ab,kw icodextrin:ti,ab,kw (glucose degradation product*) and (fluid* or solution* or dialysate*):ti,ab,kw (gdp) and (fluid* or solution* or dialysate*):ti,ab,kw (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 or #12) (#3 AND #13)
MEDLINE	<ol style="list-style-type: none"> exp Peritoneal Dialysis/ peritoneal dialysis.tw. (CAPD or CCPD or APD or PD).tw. or/1-3 Biocompatible Materials/ Dialysis Solutions/ Bicarbonates/ Lactates/

(Continued)

9. Lactic Acid/
10. Buffers/
11. biocompatib\$.tw.
12. bicarbonate\$.tw.
13. (lactate\$ or lactic acid).tw.
14. buffer\$.tw.
15. neutral pH.tw.
16. icodextrin.tw.
17. (glucose degradation product\$ and (fluid\$ or solution\$ or dialysate\$)).tw.
18. (GDP and (fluid\$ or solution\$ or dialysate\$)).tw.
19. or/5-18
20. and/4,19

EMBASE

1. Peritoneal Dialysis/
2. Continuous Ambulatory Peritoneal Dialysis/
3. peritoneal dialysis.tw.
4. (CAPD or CCPD or APD or PD).tw.
5. or/1-4
6. Biocompatibility/
7. dialysis fluid/
8. Bicarbonate/
9. Lactic Acid/
10. Buffer/
11. biocompatib\$.tw.
12. bicarbonate\$.tw.
13. (lactate\$ or lactic acid).tw.
14. buffer\$.tw.
15. neutral pH.tw.
16. icodextrin.tw.
17. (glucose degradation product\$ and (fluid\$ or solution\$ or dialysate\$)).tw.
18. (GDP and (fluid\$ or solution\$ or dialysate\$)).tw.
19. or/6-18
20. and/5,19

Appendix 2. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Random sequence generation	<i>Low risk of bias:</i> Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random).
Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence	<i>High risk of bias:</i> Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention.
	<i>Unclear:</i> Insufficient information about the sequence generation process to permit judgement.

(Continued)

Allocation concealment Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	<p><i>Low risk of bias:</i> Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes).</p> <p><i>High risk of bias:</i> Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.</p> <p><i>Unclear:</i> Randomisation stated but no information on method used is available.</p>
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study	<p><i>Low risk of bias:</i> No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.</p> <p><i>High risk of bias:</i> No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.</p> <p><i>Unclear:</i> Insufficient information to permit judgement</p>
Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors.	<p><i>Low risk of bias:</i> No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.</p> <p><i>High risk of bias:</i> No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.</p> <p><i>Unclear:</i> Insufficient information to permit judgement</p>
Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data.	<p><i>Low risk of bias:</i> No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods.</p> <p><i>High risk of bias:</i> Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.</p> <p><i>Unclear:</i> Insufficient information to permit judgement</p>
Selective reporting Reporting bias due to selective outcome reporting	<p><i>Low risk of bias:</i> The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).</p>

(Continued)

High risk of bias: Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. sub scales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear: Insufficient information to permit judgement

Other bias

Bias due to problems not covered elsewhere in the table

Low risk of bias: The study appears to be free of other sources of bias.

High risk of bias: Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem.

Unclear: Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias.

WHAT'S NEW

Date	Event	Description
27 August 2018	New citation required and conclusions have changed	New data added
27 August 2018	New search has been performed	Search strategies updated; new studies incorporated

HISTORY

Protocol first published: Issue 1, 2009

Review first published: Issue 3, 2014

Date	Event	Description
18 August 2016	Amended	Correction of table 2 results
2 May 2014	Amended	Minor edits to study names to match Renal Group's Specialised Register

CONTRIBUTIONS OF AUTHORS

- Screening of titles and abstracts: YC, HH
- Study eligibility: YC, HH
- Quality assessment, data extraction, data analysis: YC, HH, GFMS
- Writing of review: HH, YC, DJ, KW, GFMS, JC, SB
- Disagreements were resolved in consultation with DJ, SB, JC

DECLARATIONS OF INTEREST

- Htay Htay: none known
- Professor David Johnson has previously received consultancy fees, research grants, speaker's honoraria and travel sponsorships from Baxter Healthcare and Fresenius Medical Care unrelated to the preparation of this review.
- Kathryn J Wiggins: none known
- Sunil V Badve: none known
- Jonathan C Craig: none known
- Giovanni FM Strippoli: none known
- Yeoungjee Cho: none known

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Blood pressure was not analysed as an outcome in the review due to a high degree of variability and hence difficulty in ascertaining the relationship between different types of PD solutions and the control of blood pressure. Similarly, fluid balance measurement was unable to be included as an outcome in the review, primarily due to lack of reporting of relevant information in the literature.

INDEX TERMS

Medical Subject Headings (MeSH)

*Peritoneum [drug effects] [injuries]; Bicarbonates [chemistry] [therapeutic use]; Dialysis Solutions [adverse effects] [*chemistry]; Glucose [metabolism] [therapeutic use]; Hydrogen-Ion Concentration; Icodextrin [therapeutic use]; Kidney [physiology]; Peritoneal Dialysis [*methods]; Pharmaceutical Solutions [chemistry] [therapeutic use]; Randomized Controlled Trials as Topic; Urine

MeSH check words

Adult; Child; Humans