# APPENDIX 2: CHARACTERISTICS OF INCLUDED STUDIES

**BALOW 1980 (Cross-over Study)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Inpatient  Length of follow-up: None |
| Participants | Diagnosis: Research Diagnostic Criteria for schizophrenia fulfilled.  Inclusion Criteria: Only patients with a poor response to any other mode of psychiatric therapy were included in this study.  N = 8  Sex: 5M, 3F  Age: mean ~30 years  Length of illness: mean ~10 years (range = 4-25 years) |
| Interventions | Haemodialysis  Content: Vascular access via arteriovenous fistula; performed using a 0.8M2 coil dialyser with a specially prepared opacified casing to maintain blinding; blood flow rates 200ml/min; dialysate flow rate 300ml/min.  Dialysate: Standard dialysate was used except that dialysate potassium was raised to 4.0 mEq/L.  Delivered by: Unclear.  Frequency: 5hour sessions weekly.  Sham: performed using an identically appearing coil cartridge dialyser containing only tubing with a blood volume comparable to that of the active dialyser.  Treatment duration: 20 weeks |
| Outcomes | Global State: Bunney-Hamburg Global Assessment Rating using a scale of 1-15 points for psychosis, depression and mania.  Mental State: BPRS  Adverse effects/events: specific complications of haemodialysis.  Leaving the study early. |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation (selection bias) | Unclear risk | Quote: “The dialysis program involved a cross-over design in which a 10 wk bloc of active dialysis was randomly placed within a 20 wk study period.”  Comment: Authors report randomisation but to not describe how this randomisation was achieved. |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Unclear risk | Quote: “Sham procedure was performed using an identically appearing coil cartridge dialyser…”  Comment: The dialysers were covered to keep patients blinded but is unclear whether personnel were also blinded. |
| Blinding of Outcome Assessment (detection bias) All outcomes | Low risk | Quote: “Weekly ratings of patients were conducted by blinded observers.”  Comment: Probably done |
| Incomplete Outcome Data (attrition bias) All outcomes | Low risk | High dropout rate. 19 consented for the study, 8 completed the trial. Only these 8 were included in analysis. Unclear how the dropouts were analysed. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias   1. Carry Over Effect | High risk | There was no break between active or sham dialyses. There was also a potential that some patients had sham-active-sham, which raises the question of how the sham dialysis pre-active may differ from those post-active and how it would be possible to compare these patients to those that received active-sham or sham-active only. |

**CARPENTER 1983 (Cross-over study)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Outpatient  Length of follow-up: 8 weeks |
| Participants | Diagnosis: Clinical diagnosis of schizophrenia that was based on all available information and the criteria of the DSM-III; as determined by a modified version of the Present State Examination, patient had to meet Research Diagnostic Criteria for schizophrenia and score a minimum of 5 points on the Flexible Diagnostic System for schizophrenia.  Inclusion Criteria: Psychopathology of schizophrenia that had manifested at least 2 years earlier; scores on at least 4 items on the BPRS that were at the midpoint range or above. No evidence of heart disease, diabetes, allergies or contraindications to anti-coagulation.  N = 17  Sex: 10M, 7F  Age: mean 30.4 years, SD 7.4 years  Length of illness: mean 8.2 years, SD 5.2 years |
| Interventions | Haemodialysis  Content: Vascular access via arteriovenous fistula; performed using a Gambro Lundia Plate dialyser with a 1.36m2 cuprophane membrane. Blood flow rate 200ml/min. Dialysate flow rate 500ml/min.  Dialysate: Sodium 142mmol/L, potassium 4mmol/L, chloride 110mmol/L, acetate 33meq/L, calcium 1.5mmol/L and magnesium 0.75mmol/L.  Delivered by: Separate dialysis staff initiated and monitored experimental dialysis.  Frequency: 6hour sessions twice weekly  Sham: Substituted dialyser for a sham dialyser, which specifically manufactured to appear identical externally with an internal tubing segment bypassing the membranes.  Treatment duration: 16 weeks |
| Outcomes | Global State: Global Assessment Scale and the Clinical Global Impression Scale  Mental State: BPRS  Leaving the study early.  Unable to use:  Quality of life: authors used their own locally devised scale. |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation (selection bias) | Unclear risk | Quote: “…successive pairs of patients of the same sex were randomly assigned to one of two cross-over dialysis sequences…”  Comment: Authors report randomisation but to not describe how this randomisation was achieved. |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Low risk | Quote: “…sham dialyser specifically manufactured to appear identical externally…”  Quote: “Dialysers labelled only with the name of the patient and the date of use were delivered to the dialysis unit.”  Comment: Both patients and personnel were blinded to the intervention. |
| Blinding of Outcome Assessment (detection bias) All outcomes | Low risk | Quote: “…blind assessments of symptoms and social functioning…”  Comment: Probably done |
| Incomplete Outcome Data (attrition bias) All outcomes | High risk | 2 patients dropped out before completion of trial and were not included in analysis. Of the 15 that completed the trial, 2 were lost to follow up assessment and not included in the follow up outcome assessment. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias   1. Carry Over Effect | Low risk | The authors analysed the effects of order of interventions and of the interaction of treatment with order. There was a significant difference for only one outcome measure that was followed up and shown to be a short-lived effect. |

**LINKOWSKI 1979 (Parallel group)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Unclear  Length of follow-up: None |
| Participants | Diagnosis: Diagnosed as schizophrenics using diagnostic criteria for research (Reference)  Inclusion Criteria: Not described  N = 12  Sex: 10M, 2F  Age: Active HD: mean 35.1 years, SEM 1.7 years. Sham HD: mean 30.6 years, SEM 1.6 years.  Length of illness: Unclear |
| Interventions | Haemodialysis  Content: Not described  Dialysate: Not described  Delivered by: Not described  Frequency: 5hour sessions twice weekly  Sham: Not described  Treatment duration: 4 weeks |
| Outcomes | Mental State: BPRS and CPRS |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation (selection bias) | Unclear risk | Quote: “…twelve patients diagnosed as schizophrenics were randomly assigned…”  Comment: Unclear how the patients were randomised. |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Unclear risk | The author did not describe how the participants or personnel were blinded. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Outcome Assessment (detection bias) All outcomes | Low risk | Quote: “…evaluations were done before and after each session in a blind fashion…”  Comment: Probably done. |
| Incomplete Outcome Data (attrition bias) All outcomes | Low risk | All patients completed the trial and were used in the analysis. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias |  | None found |

**MALEK-AHMADI 1980 (Cross-over Study)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Inpatient  Length of follow-up: 10 days |
| Participants | Diagnosis: Patients displayed florid symptoms of schizophrenia according to DSM-II and were diagnosed based on criteria by Feighner et al. (REFERENCE)  Inclusion Criteria: patients volunteered.  N = 6  Sex: 2M, 4F  Age: mean 34 years  Length of illness: mean 10.5 years |
| Interventions | Haemodialysis  Content: Vascular access by femoral vein catheter; Cuprophan membrane dialyser used.  Dialysate: Not described  Delivered by: Dialysis technician.  Frequency: Two 4hour sessions performed one week apart.  Sham: Blood entered the dialyser unit but bypassed the dialyser.  Treatment duration: 5 weeks |
| Outcomes | Mental State: BPRS  Adverse effects/events: specific complications of haemodialysis |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation (selection bias) | Unclear risk | Quote: “…each patient randomly had two pairs of haemodialyses.”  Comment: Unclear how the patients were randomised. |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Unclear risk | The author did not describe how participants or personnel were blinded. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Outcome Assessment (detection bias) All outcomes | Low risk | Quote: “…psychiatrists blind to the random assignment of the pairs.”  Comment: Probably done |
| Incomplete Outcome Data (attrition bias) All outcomes | Low risk | All patients completed the trial and were used in the analysis. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias   1. Carry Over Effect | Unclear risk | There was one week between sham-active or active-sham dialysis, which may have removed any risk of carry over effect. However, this was not mentioned or analysed in the trial. |

**SCHULMAN 1985 (Cross-over study)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Inpatient  Length of follow-up: None |
| Participants | Diagnosis: Diagnosis of schizophrenia using research criteria by Feighner and the DSM-III.  Inclusion Criteria: Diagnosis of schizophrenia with duration of illness of at least 2 and at most 15 years; age between 20-35 years; symptoms must have persisted for at least 6 months without return to premorbid level of social adjustment; and the patient and at least one next-of-kin had to agree to participation.  N = 10  Sex: 5M, 5F  Age: mean 27 years  Length of illness: mean 8 years |
| Interventions | Haemodialysis  Content: Vascular access via arteriovenous fistula; dialysis provided with a Gambro AK 10 monitor and a parallel flow Cuprophan membrane dialyser (1.70m2). Blood flow rate 200ml/min. Dialysate flow rate 600-640ml/min.  Dialysate: Not described  Delivered by: Two specially trained nurses and a nurse’s aide under supervision of nephrologists.  Frequency: Initially twice weekly for 2 weeks, then once weekly for 8 weeks.  Sham: Same equipment was used for the same length of time. Blood but not dialysate was circulated through the dialyser.  Treatment duration: 20 weeks |
| Outcomes | Mental State: CPRS and NOSIE-30  Adverse effects/events: specific complications of haemodialysis  Leaving the study early. |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation  (selection bias) | Unclear risk | Quote: “Patients were then randomly chosen to begin with active or sham dialysis.”  Comment: Unclear how the patients were randomised. |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Low risk | Quote: “The double-blind approach was made possible by placing the patients in one room and the dialyzers and monitors in the other, so that the patients and personnel taking care of them could not see the equipment.”  Comment: Probably done. |
| Blinding of Outcome Assessment (detection bias) All outcomes | Low risk | Quote: “The raters, as well as the personnel in charge of the clinical care of the patients, has no access to vital signs or biochemical data that could reveal the type of treatment.”  Comment: Probably done. |
| Incomplete Outcome Data (attrition bias) All outcomes | Low risk | 3/10 had fistula occlusion and were not included in analysis. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias:   1. Carry Over Effect | Unclear risk | Quote: “After the completetion of the first sequence, there was a break for 3 weeks.”  Comment: The 3 week break may have removed any risk of carry over effect. However, this was not mentioned or analysed in the trial. |

**SCHULZ 1983 (Parallel Group)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Unclear  Length of follow-up: 2 weeks |
| Participants | Diagnosis: Diagnosed as either schizophrenic or schizoaffective by a psychiatrist using Research Diagnostic Criteria (REFERENCE)  Inclusion Criteria: Not described.  N = 10  Sex: 7M, 3F  Age: mean ~24 years  Length of illness: mean ~5.1 years |
| Interventions | Plasmapheresis  Content: A continuous or intermittent flow cell separator was used.  Replacement: 5% albumin in normal saline and KCl 4.0 mEq/L and calcium gluconate 4.6 mEq/L.  Delivered by: Pheresis nurses not part of the ward team.  Frequency: 2hour sessions performed 9 times in a 3week period.  Sham: Same procedure, lasting 2hours, on a cell separator but all blood components were returned.  Treatment duration: 3 weeks |
| Outcomes | Global State: Bunney-Hamburg Global Assessment  Mental State: BPRS |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation (selection bias) | Unclear risk | Quote: “…plasma exchange was performed on five patients who were randomly assigned to the active procedure.”  Comment: Unclear how the patients were randomised. |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Low risk | Quote: “The blind was maintained by a screen between the patient and the cell separator. The pheresis nurses were not part of the ward team”  Comment: Probably done. |
| Blinding of Outcome Assessment (detection bias) All outcomes | Low risk | Quote: “The patients were assessed by both psychiatrists and nurses who were blind to the nature of the pheresis procedure.”  Comment: Probably done |
| Incomplete Outcome Data (attrition bias) All outcomes | Low risk | All patients completed the trial and were used in the analysis. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias |  | None found |

**VANHERWEGHEM 1983 (Parallel Group)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Unclear  Length of follow-up: 4 weeks |
| Participants | Diagnosis: Diagnosed as schizophrenic according to the Feighner diagnostic criteria (REFERENCE)  Inclusion Criteria: Not described.  N = 19  Sex: 17M, 2F  Age: AD: mean 34.6 years, SEM 1.9 years. SD: mean 36.3 years, SEM 3.2 years.  Length of illness: AD: mean 10.3 years, SEM 1.94 years. SD: mean 8.7 years, SEM 1.6 years. |
| Interventions | Haemodialysis  Content: Vascular access by catheterising a femoral vein. A hollow fibre dialyser (0.9m2). Blood flow rate 250ml/min. Dialysate flow rate 500ml/min.  Dialysate: Not described.  Delivered by: Non-informed physicians and nurses.  Frequency: 5hour sessions performed twice weekly.  Sham: performed using a blood flow rate of 100ml/min, a hollow fibre dialyser (0.6m2) and a reduced volume of dialysate (150ml) circulating in a closed circuit so as to maintain a constant blood temperature. The external aspects of the apparatus were designed to keep the patients blind to the type of procedure.  Treatment duration: 4 weeks |
| Outcomes | Mental State: CPRS, MSS, MADS and BPRS.  Unable to use:  Radioreceptor assays of BetaH-leu5-endorphin. |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation (selection bias) | Unclear risk | Quote: “…patients were randomly assigned to active dialysis...”  Comment: Unclear how the patients were randomised. |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Low risk | Quote: “External aspects of the apparatus were so designed as to keep the patients as well as the noninformed physicians and nurses blind to the type of procedure (AD or SD).”  Comment: Probably done. |
| Blinding of Outcome Assessment (detection bias) All outcomes | High risk | Evaluators became unblinded at the end of the trial to give those having sham haemodialysis active dialysis. The data was then pooled. |
| Incomplete Outcome Data (attrition bias) All outcomes | Low risk | 24 patients were initially enrolled in the trial, however, two refused to start dialysis and two withdrew after the first dialysis. The authors remain with 19 patients. It is unclear why another patient dropped out. None of these drop outs were included in analysis.  Two patients (one undergoing AD and one undergoing SD) refused to continue after one week, and two others (one undergoing SD and one undergoing AD) after two weeks. As these patients were equally distributed between the AD and SD groups and did not differ on severity of illness, they were incorporated in analysis. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias |  | None found |

**VAN KAMMEN 1983 (Cross-over study)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Inpatient  Length of follow-up: 2 weeks |
| Participants | Diagnosis: Diagnosed with schizophrenia using research diagnostic criteria  Inclusion Criteria: On admission, patients had to manifest 4/12 differential symptoms of the International Pilot Study of Schizophrenia.  N = 8  Sex: 5M, 3F  Age: mean 30 years  Length of illness: mean 10 years |
| Interventions | Haemodialysis  Content: Vascular access by arteriovenous fistula. Performed with an Extracorporeal EX-23 coil with a Cuprophan membrane of 18μm thickness and surface area of 0.8m2 in opaque casing. Blood flow rate 200ml/min. Dialysis flow rate 300ml/min.  Dialysate: Standard haemodialysate was used, but the final potassium level was raised to 4.0 mEq/L.  Delivered by: Dialysis technician.  Frequency: 5hours sessions weekly  Sham: Sham dialyser had an identical casing to that of the active dialyser and contained tubing rather than a membrane with a blood volume equivalent to the active dialyser.  Treatment duration: 20 weeks |
| Outcomes | Mental state: National Institute of Mental Health-modified version of the BPRS.  Adverse effects/events: specific complications of haemodialysis.  Unable to use:  Autonomic activity ratings. |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation (selection bias) | Unclear risk | The author did not describe how the participants were randomised to when they would receive the 10 consecutive active dialyses, in a 20 week dialysis trial (the other dialyses were sham). |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Unclear risk | Quote: “The sham dialyser had a casing identical to that of the active dialyser…”  Comment: The patients were blinded; however, it is unclear whether the personnel were also blinded. |
| Blinding of Outcome Assessment (detection bias) All outcomes | Low risk | Quote: “Behavioural items were rated double-blind…” “The psychiatrists and nurses who rate the patients had no access to laboratory data that might have broken the blind.”  Comment: Probably done |
| Incomplete Outcome Data (attrition bias) All outcomes | Low risk | 13 patients were initially enrolled however only 8 completed the study. The authors have not included why these 5 patients dropped out of the study. Although, they were not included in the analysis. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias   1. Carry Over Effect | High risk | There was no break between active or sham dialyses. There was also a potential that some patients had sham-active-sham, which raises the question of how the sham dialysis pre-active may differ from those post-active and how it would be possible to compare these patients to those that received active-sham or sham-active only. |

**WAGEMAKER 1983/1984 (Parallel Group)**

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| Methods | Allocation: randomised  Blinding: double-blind  Location: Unclear  Length of follow-up: None |
| Participants | Diagnosis: Diagnosis of schizophrenia using the life-term version of the Schedule for Affective Disorders and Schizophrenia, undertaken by the principal investigator.  Inclusion Criteria: Patients exhibited at least an average IQ; had experienced a psychotic episode before age 25 years; had previously been hospitalised with a diagnosis of schizophrenia.  N = 24  Sex: 12M, 12F  Age: mean ~27 years  Length of illness: Unknown |
| Interventions | Haemodialysis  Content: Performed with hollow fibre filters that were 14μm thick, 2m2 surface area.  Dialysate: Not described.  Delivered by: Dialysis nurses.  Frequency: 6hours sessions performed twice weekly.  Sham: Dialysis units were outwardly identical.  Treatment duration: 8 weeks |
| Outcomes | Global state: Modified Clinical Global Impression Scale.  Mental state: SADS (version C and PD), BPRS and Symptom Checklist-90 |

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| Domain | Review Authors’ Judgement | Support for Judgement |
| Random Sequence Allocation (selection bias) | Unclear risk | Quote: “Each group contained two male and two female patients, with one individual from each sex selected randomly to receive active and the other sham to receive sham dialysis.”  Comment: Unclear how the patients were randomised. |
| Allocation Concealment (selection bias) | Unclear risk | The author did not describe how the allocation of the participants was concealed. Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’. |
| Blinding of Participants and Personnel (performance bias) All outcomes | Low risk | Quote: “Active and sham dialysis filters were supplied by the manufacturer and were outwardly identical.” “The patients and all members of the research team, including the principal investigator and the dialysis nurses, were blind to the treatment modality…”  Comment: Probably done |
| Blinding of Outcome Assessment (detection bias) All outcomes | Low risk | Quote: “The patients and all members of the research team, including the principal investigator and the dialysis nurses, were blind to the treatment modality…”  Comment: Probably done |
| Incomplete Outcome Data (attrition bias) All outcomes | High risk | One patient did not complete all of the tools to measure outcome for every week of the trial. An additional patient informed the authors they had been taking their medication throughout the trial. 3 patients experienced fistula difficulties and were dropped from the trial in the 5th, 6th and 7th weeks. However, all of these patients were included in the analysis. |
| Selective Reporting (reporting bias) | Unclear risk | No protocol for the study is available and all expected outcomes reported in the methods are reported as planned. |
| Other Sources of Bias |  | None found |