Health technology assessment of the different dialysis modalities in Norway

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Health technology assessment HTA

kunnskapssenteret

Background: During the last ten years, the number of dialysis patients has doubled in Norway. After a request from The Norwegian Directorate of Health we performed a Health Technology Assessment comparing efficacy, safety and cost-effectiveness of different dialysis modalities. **Clinical findings:** •No significant differences in mortality, in quality of life or in infections. •Significantly fewer hospitalisation days per patients per year in the hemodialysis hospital group versus the peritoneal dialysis at home group. **Economic evaluation:** •In our model analyses all dialysis modalities were almost equally effective. •Hemodialysis at home was the most effective and cost-effective alternative compared to all other hemodialysis modalities from both healthcare and societal perspectives. •Peritoneal dialysis was the least costly, and hence the most cost-effective alternative compared to all hemodialysis modalities. •The results of our sensitivity analysis showed that cost data had the greatest impact on the results' uncertainty.

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We would like to thank all contributors for their expertise in this project. Norwegian Knowledge Centre for the Health Services assumes final responsibility for the content of this report.

Norwegian Knowledge Centre for the Health Services
Oslo, December 2013

Key messages

During the last ten years, the number of dialysis patients has doubled in Norway. After a request from The Norwegian Directorate of Health we performed a Health Technology Assessment comparing efficacy, safety and cost-effectiveness of the different dialysis modalities 1) Hemodialysis carried out in hospital, 2) self-care hemodialysis in hospital, 3) hemodialysis in satellite unit (nursing home, local medical centre), 4) hemodialysis at home and 5) peritoneal dialysis at home for patients with end-stage renal failure requiring dialysis in Norway. Our outcomes were mortality, complications that require special measures and quality of life.

Clinical findings

Of 21 possible comparisons only six had published data. For the comparisons with published data and low quality of the evidence, we found:

- no significant differences in mortality, in quality of life or in infections
- significantly fewer hospitalisation days per patients per year in the hemodialysis hospital group versus the peritoneal dialysis at home group

Economic evaluation

- In our model analyses all dialysis modalities were almost equally effective.
- Hemodialysis at home was the most effective and cost-effective alternative compared to all other hemodialysis modalities from both healthcare and societal perspectives.
- Peritoneal dialysis was the least costly, and hence the most cost-effective alternative compared to all hemodialysis modalities.
- The results of our sensitivity analysis showed that cost data had the greatest impact on the results' uncertainty.

Title:
Health technology assessment of the different dialysis modalities in Norway

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Type of publication:
Health technology assessment

Health technology assessment (HTA) is a multidisciplinary process that summarizes information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the development of safe, effective health policies that are patient focused and that seek to achieve best value.

Doesn't answer everything:

- Excludes studies that fall outside of the inclusion criteria
- No recommendations

Publisher:
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Executive summary

Background

About 11 % of the Norwegian population has chronic kidney disease (CKD). Some of these persons develop end-stage renal failure with the need for renal replacement therapy (RRT). The number of dialysis patients in Norway has increased from 241 in 1990 to 1240 in 2012. With the expected demographic development of increased numbers of elderly people, people with high blood pressure, cardiovascular diseases and/or diabetes, one can anticipate a further increase in the number of people with chronic renal failure in need of RRT in the future.

Generally, there are two different types of dialysis: hemodialysis (HD) and peritoneal dialysis (PD). In Norway hemodialysis performed in hospitals (satellites included) is the most frequently used modality (84.2%), whereas peritoneal dialysis at home makes up for 15.8%. Only 11 patients (0.8%) received hemodialysis at home by the end of 2012 (1).

Upon a request from The Norwegian Directorate of Health we performed a Health Technology Assessment comparing efficacy, safety and cost-effectiveness of the different dialysis modalities in Norway. This request has its background in "The Norwegian action plan for the prevention and treatment of chronic kidney disease" (2011-2015)".

With the increasing number of dialysis patients expected, there is a need to compare both cost-effectiveness and safety data for the different dialysis modalities used in Norway today.

Objective

Our objective was to perform a Health Technology Assessment comparing efficacy, safety and cost-effectiveness of the different dialysis modalities 1) Hemodialysis carried out in hospital, 2) self-care hemodialysis in hospital, 3) hemodialysis in satellite units (nursing home, local medical centre), 4) hemodialysis at home and 5) peritoneal dialysis at home for patients above 18 years with end-stage renal failure requir-

ing dialysis in Norway. Our outcomes were mortality, complications that require special measures and quality of life.

Method

We performed a systematic literature search for systematic reviews, randomized controlled trials and controlled observational studies to find information about mortality, complications that require special measures and quality of life for the specified dialysis modalities. The quality of the evidence for each outcome was assessed by GRADE.

We performed a cost-utility analysis (CUA) where relevant costs were expressed in 2012 Norwegian kroner (NOK), and effects were expressed in quality-adjusted life-years (QALYs). The analysis was carried out from both a societal and healthcare perspective.

In order to assess the cost-effectiveness of different dialysis modalities, a decision analytic model was developed in TreeAge pro ® 2012. The model is of the Markov type, in which a cohort of patients is followed over a given period of time. A Markov model was considered appropriate as end stage renal failure (ESRF) is a chronic condition requiring continuous treatment.

The results were expressed as mean incremental cost-effectiveness ratio (ICER) and mean incremental net health benefit.
Uncertainties in model parameters were handled by performing one-way (tornado diagram) and probabilistic sensitivity analyses, designed as a Monte Carlo simulation, with 1000 iterations.

Results

In this HTA we have systematically reviewed and summarized the clinical results from 18 publications reporting results from two randomized controlled studies and 17 observational studies.
We have further performed an economic evaluation to examine the relative cost-effectiveness in a Norwegian setting of different dialysis modalities from both healthcare and societal perspectives in patients with end stage renal disease.

Clinical findings

Of 21 possible comparisons only six had published data.
For the comparisons with published data and low quality of the evidence, we found:

- no significant differences in mortality, in quality of life or in infections
- significantly fewer hospitalisation days per patient per year in the hemodialysis hospital group versus the peritoneal at home dialysis group

Economic evaluation

- From a healthcare perspective: Hemodialysis at home was more effective and less costly (the dominant modality) relative to hemodialysis at hospital and hemodialysis in satellite. Hemodialysis at home was more costly and more effective than self-care hemodialysis and peritoneal dialysis although the incremental cost-effectiveness ratios (ICER; NOK 1,651,099 and NOK 4,344,526, respectively) were clearly above the suggested threshold for cost-effectiveness of NOK 588,000 per QALY gained.
- From a societal perspective: Hemodialysis at home dominated all other hemodialysis modalities (i.e. hemodialysis in hospital, self-care hemodialysis and hemodialysis in satellite). Hemodialysis at home was more costly and more effective relative to peritoneal dialysis, but the ICER (NOK 2,657,211) was above the suggested threshold.
- The results of our sensitivity analysis showed that cost data had the greatest impact on the results' uncertainty.

Discussion

Most of our documentation regarding effectiveness of the different dialysis modalities came from controlled observational studies. Since observational studies lack randomization they are normally deemed to have a greater potential for varying patient characteristics across groups at baseline. We have therefore only assessed studies where the groups did not differ significantly in comorbidity at baseline.

For this HTA we were asked specifically to focus on the type of dialysis performed and the delivery location. Consequently, we could not examine differences in dialysis frequency, dialysis adequacy, residual function or dialysis equipment, all of which could possibly have influenced our results.

Lack of data comparing different hemodialysis modalities (with regard to treatment location) was the most important limitation of this study. This limitation was relevant to all parameters, *i.e.* effect, complications, quality of life and costs.

Little research exists examining the costs of different dialysis modalities in Norway, making it difficult to obtain reliable cost information for the different modalities, particularly home and satellite, and with regard to geographical conditions and existing infrastructure in different regions. Although we have tried to conduct our analyses based on best available data, and have incorporated uncertainty around cost estimates in the sensitivity analysis, the cost estimates need to be treated with some caution.

In several cases, efficacy parameters used in the model are based on meta-analyses with no significant results. In health economic evaluation it is a common practice to include no significant differences since effect estimates from clinical studies themselves are considered to be the most likely outcome, and because it is assumed that the probability distributions represent the actual uncertainty.

Conclusion

In our model analyses all dialysis modalities were almost equally effective. When effects are combined with cost, hemodialysis at home was the most cost-effective alternative among the hemodialysis modalities. Peritoneal dialysis was the least expensive and hence the most cost-effective alternative compared to all hemodialysis modalities.

Hovedfunn (norsk)

I løpet av de siste ti årene er antall dialyse-pasienter i Norge fordoblet. Etter en forespørsel fra Helsedirektoratet har vi utført en metodevurdering hvor vi sammenligner effekt, sikkerhet og kostnadseffektivitet av ulike dialysemetoder i Norge for pasienter over 18 år med dialysetrengende kronisk nyresvikt. Følgende dialysemetoder er sammenlignet: 1) Hemodialyse (HD) i sykehus, 2) selvadministrert HD i sykehus, 3) HD i satelittenheter (sykehjem, distriktsmedisinske sentre), 4) HD hjemme og 5) peritoneal dialyse (PD) hjemme. Vi undersøkte effekten i forhold til dødelighet, komplikasjoner som krever spesielle tiltak og livskvalitet.

Kliniske resultater

Av 21 mulige sammenligninger var det kun seks som hadde publiserte data. For sammenligninger med publiserte data og lav kvalitet på dokumentasjonen, fant vi:

- ingen signifikante forskjeller i dødelighet, livskvalitet eller infeksjoner
- signifikant færre sykehusdager per pasient per år i gruppen som fikk hemodialyse på sykehus versus de som fikk peritonealdialyse hjemme.

Økonomiske evalueringer

- I vår modellanalyse var alle dialysealternativene omtrent like effektive.
- Hemodialyse hjemme var det mest effektive og kostnadseffektive alternativet sammenlignet med alle de andre hemodialysemetodene både fra et helsetjeneste- og samfunnsperspektiv.
- Peritonealdialyse kostet minst, og var dermed det mest kostnadseffektivte alternativet sammenlignet med alle hemodialysemetodene.
- Resultater fra våre sensitivitetsanalyser viste at kostnadsdata hadde størst påvirkning på resultatenes usikkerhet.

Tittel:
Effekt og kostnadseffektivitet av ulike dialysemodaliteter hos pasienter med alvorlig nyresvikt i Norge

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Publikasjonstype:
Metodevurdering

En metodevurdering er resultatet av å
- innhente
- kritisk vurdere og
- sammenfatte relevante forskningsresultater ved hjelp av forhåndsdefinerte og eksplisitte metoder.

Minst ett av følgende tillegg er også med:
helseøkonomisk evaluering, vurdering av konsekvenser for etikk, jus, organisasjon eller sosiale forhold

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Svarer ikke på alt:

- Ingen studier utenfor de eksplisitte inklusjonskriteriene
- Ingen anbefalinger

Hvem står bak denne rapporten?

Kunnskapssenteret har skrevet rapporten på oppdrag fra Helsedirektoratet

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Når ble litteratursøket utført?

August 2013

Sammendrag (norsk)

Bakgrunn

Om lag 11 % av den norske befolkningen har kronisk nyresykdom (KNS). Noen av disse personene utvikler alvorlig nyresvikt med behov for nyreerstattende behandling. Antallet dialysepasienter i Norge har økt fra 241 i 1990 til 1240 i 2012. Med den forventede demografiske utviklingen med økende antall eldre, økende antall mennesker med høyt blodtrykk, hjerte- og karsykdom og/eller diabetes kan en forvente en ytterligere økning i antall mennesker med kronisk nyresvikt som har behov for nyre-erstattende behandling i fremtiden.

Generelt er det to typer dialyse: hemodialyse (HD) og peritonealdialyse (PD). I Norge er hemodialyse utført i sykehus (inkludert satellitter) mest brukt (84,2 %), mens peritonealdialyse hjemme utgjør 15,8 %. Kun 11 pasienter (0,8 %) fikk HD hjemme ved slutten av 2012.

Etter en forespørsel fra Helsedirektoratet har vi utført en metodevurdering hvor vi sammenligner effekt, sikkerhet og kostnadseffektivitet av ulike dialysemetoder i Norge. Denne forespørselen hadde sin bakgrunn i ”Handlingsplan for forebygging og behandling av kronisk nyresykdom (2011-2015)".

Med den forventende økningen i antall dialysepasienter så er det et behov for å sammenligne både kostnadseffektivitet og sikkerhetsdata for de ulike dialysemetodene som brukes i Norge i dag.

Problemstilling

Vårt formål var å utføre en metodevurdering hvor vi sammenligner effekt, sikkerhet og kostnadseffektivitet i Norge av ulike dialysemetoder for pasienter over 18 år med dialysetrengende kronisk nyresvikt. Følgende dialysemetoder er sammenlignet: 1) Hemodialyse i sykehus, 2) selvadministrert HD i sykehus, 3) HD i satellittenheter (sykehjem, distriktsmedisinske sentre), 4) HD hjemme og 5) peritonealdialyse hjemme. Våre effektmål var dødelighet, komplikasjoner som krever spesielle tiltak og livskvalitet.

Metode

Vi gjorde et systematisk litteratursøk for systematiske oversikter, randomiserte kontrollerte studier og kontrollerte observasjonsstudier for å finne informasjon om dødelighet, komplikasjoner som krever spesielle tiltak og livskvalitet for de spesifiserte dialysemetodene. Kvaliteten på resultatet for hvert effektmål ble vurdert ved hjelp av GRADE.

Den helseøkonomiske evalueringen ble gjort som en kostnadseffektivitetsanalyse der relevante kostnader ble målt i norske 2012-kroner, og effekten ble målt i kvalitetsjusterte leveår. Analysen ble gjort både fra et helsetjenesteperspektiv og et tilnærmet samfunnsperspektiv.

Den helseøkonomiske evalueringen ble basert på en beslutningsmodell utviklet i promgramvaren TreeAge pro ® 2012. Modellen ble designet som en Markov modell, hvor en kohort av pasienter følges over en gitt tidsperiode. En Markov modell var egnet siden terminal nyresvikt er en kronisk tilstand som krever kontinuerlig behandling.

Resultatene ble uttrykt som kostnadseffektivitetsbrøk (ICER) og gjennomsnittlig inkrementell netto helsenytte. Vi utførte enveis- og probabilistiske sensitivitetsanalyser, en Monte Carlo simulering med 1000 iterasjoner, for å få et inntrykk av usikkerheten knyttet til resultatene.

Resultat

I denne metodevurderingen har vi systematisk gjennomgått og sammenfattet de kliniske resultatene fra 18 publikasjoner som rapporterte resultater fra to randomiserte kontrollerte studier og 17 kontrollerte observasjonsstudier.
Vi har videre utført en økonomisk evaluering for å undersøke den relative kostnadseffektiviteten av forskjellige dialysemetoder i Norge både fra et helsetjeneste- og samfunnsperspektiv hos pasienter med alvorlig nyresvikt.

Kliniske resultater

Av 21 mulige sammenligninger var det kun seks som hadde publiserte data. For sammenligninger med publiserte data og lav kvalitet på dokumentasjonen, fant vi:

- ingen signifikante forskjeller i dødelighet, livskvalitet eller infeksjoner
- signifikant færre sykehusdager per pasient per år i gruppen som fikk hemodialyse på sykehus versus de som fikk peritoneal dialyse hjemme

Økonomiske evalueringer

- Fra et helsetjenesteperspektiv: Hemodialyse hjemme hadde lavere kostnader og høyere helsegevinst (dominant modalitet) sammenlignet med

hemodialyse i sykehus og i satellitt. Hemodialyse hjemme var dyrere og hadde høyere helsegevinst enn selvadministrert hemodialyse på sykehus og peritonealdialyse selv om de inkrementelle kostnadseffektivitetsbrøkene (ICER; henholdsvis NOK 1 651 099 og NOK 4 344 526) var klart over den grenseverdien som har vært foreslått for vurdering av kostnadseffektivitet i helsevesenet (NOK 588 000 per vunnet QALY).

- Fra et samfunnsperspektiv: Hemodialyse hjemme dominerte alle de andre hemodialysemetodene (dvs. hemodialyse på sykehus, selvadministrert hemodialyse i sykehus og hemodialyse i satellitt). Hemodialyse hjemme var mer kostbart og mer effektivt i forhold til peritonealdialyse, men ICER (NOK 2 657 211) var over den grenseverdien som har vært foreslått for vurdering av kostnadseffektivitet i helsevesenet.
- Resultatene fra våre sensitivitetsanalyser viste at kostnadsdata hadde størst påvirkning på resultatenes usikkerhet.

Diskusjon

Det meste av vår dokumentasjon vedrørende effekten av de ulike dialysemetodene kom fra kontrollerte observasjonsstudier. Fordi observasjonsstudier ikke er randomiserte er de vanligvis ansett for å ha et større potensiale for variasjoner i pasientkarakteristikkene mellom gruppene ved studiestart. Vi har derfor kun vurdert studier hvor gruppene ikke hadde signifikante forskjeller i tilleggssykdommer ved studiestart, eller studier som hadde justert for dette i sine analyser.

I denne metodevurderingen var vi bedt spesifikt om å fokusere på dialysetype og på hvor dialysen ble utført. Som en konsekvens av dette kunne vi ikke undersøke forskjeller i dialysefrekvens, dialyseeffekt, restfunksjon eller dialyseutstyr. Alle disse faktorene kunne ha påvirket våre resultater.

Mangel på data som sammenligner ulike hemodialysemetoder, med hensyn på behandlingssted, var den viktigste begrensningen i vår metodevurdering. Denne begrensningen var relevant for alle parametere, dvs effekt, komplikasjoner, livskvalitet og kostnader.

Det finnes lite forskning som undersøker kostnader for ulike dialysemetoder i Norge. Dette gjør det vanskelig å skaffe pålitelig informasjon om kostnader for de forskjellige alternativene, spesielt for dialyse hjemme og i satellitter, samt informasjon om geografiske forhold og eksisterende infrastruktur i de ulike regioner. Selv om vi har forsøkt å gjøre vår analyse basert på de best tilgjengelige data og har inkorporert usikkerhet rundt kostnadsanslagene i sensitivitetsanalysen, så er det behov for å betrakte disse med noe forsiktighet.

I flere tilfeller er effektparameterne som er brukt i modellen basert på meta-analyser med ikke signifikante resultater. I helseøkonomiske vurderinger er det vanlig praksis å inkludere ikke signifikante forskjeller. Dette fordi det er effektestimatet i seg selv som er vurdert å være det mest sannsynlige utfallet og fordi man antar at sannsynlighetsfordelingene representerer den faktiske usikkerheten på en rimelig god måte.

Konklusjon

I våre modellanalyser var alle dialysemetodene, uavhengig av hvor de ble utført, omtrent like effektive. Når effekten kombineres med kostnad ble hemodialyse hjemme den mest kostnadseffektive hemodialysemetoden. Peritonealdialyse kostet minst og var dermed det mest kostnadseffektivte alternativet sammenlignet med alle hemodialysemetodene.

Nasjonalt kunnskapssenter for helsetjenesten fremskaffer og formidler kunnskap om effekt av metoder, virkemidler og tiltak og om kvalitet innen alle deler av helsetjenesten. Målet er å bidra til gode beslutninger slik at brukerne får best mulig helsetjenester. Kunnskapssenteret er formelt et forvaltningsorgan under Helsedirektoratet, men har ikke myndighetsfunksjoner og kan ikke instrueres i faglige spørsmål.

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Glossary and abbreviation

	Explanation
APD	Automated peritoneal dialysis
CAPD	Continuous ambulatory peritoneal dialysis
CI	**Confidence interval.** A measure of uncertainty around the results of a statistical analysis that describes the range of values within which we can be reasonably sure that the true mean effect lies. Wider intervals indicate lower precision; narrower intervals, greater precision.
CUA	**Cost-utility analysis.** An economic evaluation in which health consequences are measured in **QALY**s.
Erythropoietin	Erythropoietin is a hormone produced by the kidney that promotes the formation of red blood cells by the bone marrow. Patients with end stage renal disease do not produce this hormone. Erythropoietin as a substitute was introduced about 1995.
EQ-5D	**European Quality of Life-5 Dimensions.** EQ-5D is a standardized instrument for use as a measure of health outcome.
HD	Hemodialysis
HR	**Hazard ratio.** Ratio of hazard rates. Ratios above 1 indicate increased instantaneous rate of an event. Ratios below 1 indicate a decrease in event rates.
HTA	**Health technology assessment.** Multi-disciplinary overview of a policy question, contain a systematic review of the technology and an economic evaluation, and often also other implications like ethical, legal and organizational consequences
Healthcare perspective	Economic evaluation from a healthcare perspective will consider only the costs and consequences specifically related to the

	healthcare sector (direct costs), *e.g.* staff costs, capital costs, drug acquisition costs.
ICER	**Incremental cost-effectiveness ratio**. The ratio of the difference in costs between two alternative health technologies to the difference in effectiveness between these two technologies. $ICER = \frac{Cost_{\text{intervention}} - Cost_{\text{comparator}}}{Effect_{\text{intervention}} - Effect_{\text{comparator}}} = \frac{\Delta C}{\Delta E}$
KDQL	Kidney Disease Quality of Life
INHB	**Incremental Net Health Benefit.** In a decision-making process, a positive INHB suggests that the intervention represents good value for money $INHB: \Delta E - (\Delta C/\lambda) > 0$
INMB	**Incremental Net Monetary Benefit.** In a decision-making process, a positive INMB suggests that the intervention represents good value for money. $INMB: \lambda \bullet \Delta E - \Delta C > 0$
PD	Peritoneal dialysis
PSA	**Probabilistic sensitivity analysis.** An analysis of the uncertainty related to all parameters in a decision analytic model. Typically performed by Monte Carlo simulation, hence by drawing values from probability distributions for all parameters simultaneously.
QALY	**Quality-adjusted life-year.** A measure of health outcomes that combines quantity and quality of life by assigning to each year of life a weight from 1 (perfect health) to 0 (state judged equivalent to death) dependent on the individual's health related quality of life during that year
RCT	**Randomized controlled trial.** An experiment in which investigators use randomization to allocate participants into the groups that are being compared. Usually allocation is made at the level of individuals, but sometimes it is done at group level e.g. by schools or clinics. This design allows assessment of the relative effects of interventions.
RR	**Relative risk / risk ratio.** The relative risk is the absolute risk (AR) in the intervention group divided by the AR in the control group. It is to be distinguished from odds ratio (OR), which is the ratio of events over non-events in the intervention group over the

	ratio of events over non-events in the control group.
Satellite unit	Nursing home, local medical centre
Self-care HD	Self-care hemodialysis carried out in hospital
SF-36	The Short Form (36) Health Survey. The SF-36 consists of eight scaled scores: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health
Societal perspective	Societal perspective will incorporate all elements, including in the analysis the costs and consequences that accrue not only to the patient but also those costs that accrue to the health care sector and other members of society (indirect costs), *e.g*. loss of leisure time, loss of productivity.
SR	**Systematic review.** A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyze and summarize the results of the included studies.
Statistically significant	Means that the findings of a study are unlikely to have arisen because of chance. Significance at the commonly cited 5% level ($P < 0.05$) means that the observed difference or greater difference would occur by chance in only 1/20 similar cases. Where the word "significant" or "significance" is used without qualification in the text, it is being used in this statistical sense.
WTP (λ)	**Willingness to pay**. A pre-specified threshold of what society is willing to pay for a given health unit (e.g. QALY or life year).

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Preface

This project was commissioned by The Norwegian Directorate of Health, which requested that we compare efficacy and cost-effectiveness of the different dialysis modalities for patients with end-stage renal failure requiring dialysis in Norway.

The results of this HTA report may be used as scientific documentation for the recommendations on the selection of the dialysis modalities for patients with end-stage renal failure.

Eva Pike was lead reviewer for the clinical evaluation and Vida Hamidi lead the health economic evaluation. We will thank the external experts Aud-Eldrid Stenehjem, Head of department of Nephrology,Oslo University Hospital, Ullevål; Ann Lisbeth Sandvik, Senior adviser, Department of Economy and Analysis, The Norwegian Directorate of Health and Therese Dalen, Dialysis clinical nurse specialist, The Norwegian Nurses Organisation. Peer-review was performed internally by Lene Kristine Juvet (researcher) and Gunhild Hagen (health economist); and externally by Cecilia Øien (Chairman of Norwegian Renal Medical Association) and Ivar Sønbø Kristiansen (Professor of Institute of Health Management and Health Economics). We thank them for valuable contribution.

The project group consisted of the following persons affiliated with the Norwegian Knowledge Centre for the Health Services:

- Tove Ringerike, Researcher,
- Torbjørn Wisløff, Statistician,
- Arna Desser, Researcher,
- Ingrid Harboe, Research librarian,
- Marianne Klemp, Head of Health Economics and Drugs Unit,

The aim of this report is to support well-informed decisions in health care that lead to improved quality of services. The evidence should be considered together with other relevant issues, such as clinical experience and patient preference.

Gro Jamtvedt	Marianne Klemp	Eva Pike	Vida Hamidi
Department Director	*Head of Unit*	*Lead reviewer, Clinical evaluation*	*Lead health Economist*

Objective

To compare efficacy, safety and cost-effectiveness of the different dialysis modalities in Norway for patients with end-stage renal failure requiring dialysis:
1) hemodialysis (HD) carried out in hospital,
2) self-care HD in hospital,
3) HD in satellite unit (nursing home, local medical centre),
4) HD at home and
5) peritoneal dialysis at home

Background

About 11 % of the Norwegian population has chronic kidney disease (CKD) (2) (NKF-K/DOQI) (3;4). Some of these persons develop end-stage renal failure with the need for renal replacement therapy (RRT). Renal transplantation is a common treatment (1), but not all patients with a need for RRT can get a graft. At the end of 2012, 4448 persons (886.5 persons per million residents) received RRT in Norway, 1240 of those were on chronic dialysis, and more than 50% of those who got chronic dialysis in 2012, were considered not suitable for transplantation; i.e. 649 persons (1).

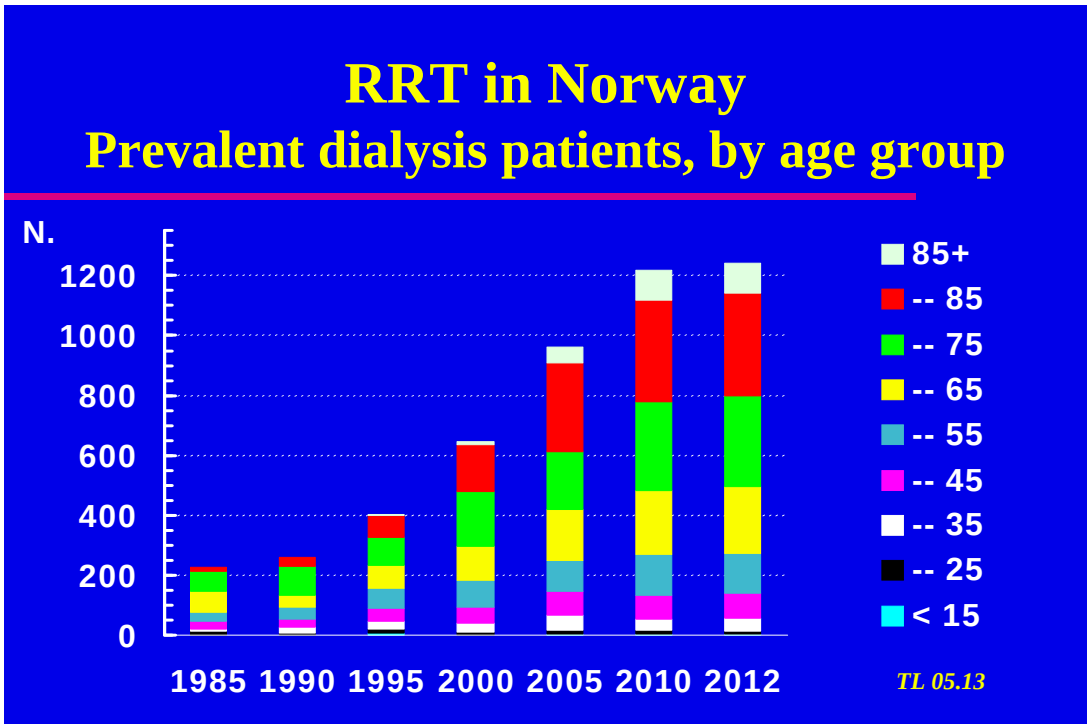


Figure 1 *Persons who received RRT in Norway at end of 2012 (1).*

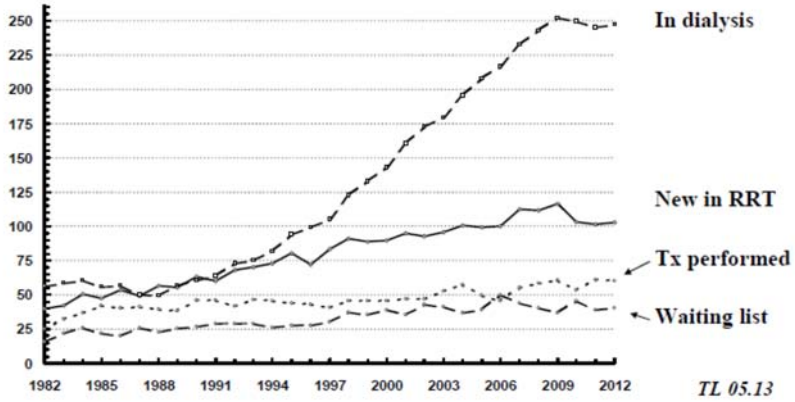


Figure 2 *Renal replacement therapy in Norway, status by end of year-patients pr mill. inhabitants (1).*

The number of dialysis patients in Norway has increased from 241 in 1990 to 1240 in 2012 (1). With the expected demographic development, with increased number of elderly people, people with high blood pressure, cardiovascular diseases and/or diabetes, one can anticipate an increase in the number of people with chronic renal failure in need of RRT in the future (1;5).

Generally, there are two different types of dialysis: hemodialysis (HD) and peritoneal dialysis (PD). In hemodialysis the circulating blood is filtered through a semipermeable membrane in a machine which removes waste products and water from the blood. In peritoneal dialysis the patient's own peritoneal membrane inside the abdominal cavity is used as the dialysis membrane (5). Hemodialysis can be performed in hospitals, different medical institutions or at home, whereas peritoneal dialysis (PD) is a home based dialysis. Hemodialysis is usually performed 3-5 hours 3 times a week (5), whereas PD at home is continuously performed with change of fluid 4 times per 24 hours (CAPD) or by use of a machine that exchanges the fluid during the night (APD) (5).

In Norway hemodialysis performed in hospitals (satellites included) is the most frequently used modality (84.2%), whereas PD at home makes up for 15.8%. Only 11 patients (0.8%) received HD at home by the end of 2012 (1). The choice of dialysis modality depends on patients comorbidity, suitability for renal transplantation and for those on the waiting list, expected time to transplantation.

All counties, except one, have a central renal unit and some have two, further some counties have satellite units run in close contact with the central unit. There is only one transplant centre in Norway at Oslo University Hospital, Rikshospitalet. Pre-transplant work-up, as well as post-transplant follow-up beyond 10 weeks, is handled by the county-centres.

To compare efficacy and cost-effectiveness of the different dialysis modalities for patients with end-stage renal failure requiring dialysis in Norway, The Norwegian

Directorate of Health requested The Norwegian Knowledge Centre for the Health Services (NOKC) for a health technology assessment (HTA). This request has its background in "Handlingsplan for forebygging og behandling av kronisk nyresykdom/The action plan for prevention and treatment of chronic kidney disease (2011-2015)" (5).

This plan aims that patients with chronic kidney disease should be offered good and individual renal replacement therapy, independent of residence, socioeconomic situation and ethnicity, and furthermore that the traveling distance between home and dialysis centre should not be more than one hour.
With the increasing number of dialysis patients expected, there is a need to compare both cost-effectiveness- and safety data for the different dialysis modalities used in Norway today.

Introduction to health technology assessment (HTA)

The basis of an HTA is a systematic review and evaluation of scientific literature on efficacy and safety of different therapeutic interventions or diagnostics. The HTA may also include economic evaluations and a discussion regarding ethical, social, legal and organizational aspects depending on the question under evaluation.

This HTA consists of data from a systematic review summarizing efficacy and safety data and an economic model-based evaluation relevant for the Norwegian setting.

Introduction to Economic Evaluations of Health Care Programmes

The basic task of any economic evaluation is to identify, measure and compare costs and consequences of the alternatives under consideration in an incremental analysis—one in which the differences in costs are compared with differences in consequences (6). Hence, results of economic evaluations can be expressed as an incremental cost-effectiveness ratio (ICER), which is defined by the following equation:

$$ICER = \frac{Cost_{\text{intervention}} - Cost_{\text{comparator}}}{Effect_{\text{intervention}} - Effect_{\text{comparator}}} = \frac{\Delta C}{\Delta E}$$

Because the health care sector, like society in general, is restricted by scarce resources and budget constraints, economic evaluations are important tools for decision makers facing questions of how to prioritize treatments and maximize health benefits using scarce resources. For an economic evaluation to be meaningful in a decision making process, the ICER must be judged with regard to a ceiling ratio that

reflects the decision maker's maximum willingness to pay (WTP) for a health gain. The decision rule for an economic evaluation can therefore be expressed as

$$\frac{\Delta C}{\Delta E} < \lambda$$

where λ equals WTP, and means that if the ICER of an intervention is below the ceiling ratio, introducing the intervention represents good value for money. Because the ICER has poor statistical properties, ICERs are often rearranged to express either incremental net monetary benefit (INMB) or incremental net health benefit (INHB), which yields the following decision rules related to INMB or INHB.

INMB: $\lambda \bullet \Delta E - \Delta C > 0$

INHB: $\Delta E - (\Delta C/\lambda) > 0$

An intervention can in other words be considered cost-effective if it yields a positive INHB or INMB.

Economic evaluations are often based on decision models (such as decision trees, Markov models, etc.) that calculate results based on various input parameters in the model. Because there are always uncertainties related to the values of these parameters, sensitivity analysis is an important feature of any economic evaluation based on a decision model framework. In short, sensitivity analysis illustrates how much the results vary when model parameters are changed. Sensitivity analyses can be performed in many ways, with one-way or two-way sensitivity analysis being common approaches. These entail changing, respectively, one or two model-parameters at a time while all of the other model-parameters are held constant in order to determine how much impact the variation in these parameters has on the results. One-way sensitivity analyses are often presented as tornado-diagrams, which identify and illustrate the model-parameters that have the highest impact on the results.

Another important kind of sensitivity analysis is referred to as probabilistic sensitivity analysis (PSA). The advantage of PSA is that it makes it possible to take the uncertainties of all of the model-parameters into account simultaneously. The basic approach in PSA is to assign appropriate probability distributions to the model-parameters, which makes it possible to replace the "fixed" values of the parameters with values generated by random draws from the distributions. Doing this repeatedly, with a specified number of iterations, makes it possible to estimate the probabilities that alternative interventions are cost-effective subject to different ceiling values of WTP. The calculation is based on the alternative that renders the highest values of NMB or NHB. Results from PSAs are often presented as scatter plots, which show point estimates of the ICER for all iterations in the cost-effectiveness plane, and also

as cost-effectiveness acceptability curves (CEACs), which show the probability of the alternatives being cost-effective subject to changing values of WTP.

Another result from PSA is the expected value of perfect information (EVPI). This is a number that indicates the value to society of having more accurate information about the decision, given a WTP. If EVPI for a given population seems large, it might be of interest to determine for which parameters it would be most useful to obtain additional data. Expected value of perfect information for parameters is a more time-consuming analysis that can help determine for which single parameters or groups of parameters it is most cost-effective to conduct new research.

In short, making a model probabilistic means that it is possible to estimate the uncertainty associated with a decision to implement alternative interventions, and also provides a possibility of estimating the value of collecting additional information from new research.

Priority setting criteria

According to Norwegian policy documents (7;8), a treatment should be prioritized if the following criteria are met:

- *The disease is severe:* A disease is considered severe to the degree that it causes pain and discomfort, loss of physical, psychological and social function and if it limits the individual in his or her daily activities. Severity is also evaluated according to the risk increase the disease entails in terms of death, disability and discomfort, if treatment is postponed.

- *The treatment is effective:* The patient should be expected to benefit from treatment in terms of longevity or improved quality of life of certain duration. The treatment effectiveness should also be well documented.

- *The treatment is cost-effective:* The additional costs of the treatment should be reasonable compared to the additional benefits.

The policy documents mentioned above give no guidance as to what constitutes a "reasonable" relationship between costs and effectiveness for a given health intervention. The Directorate of Health, however, has recommended a preliminary estimate of NOK 500 000 per statistical life year in full health (9;10). This value was based on Norwegian price levels in 2005, and translates to 588 000 for 2012 (9). However, there is no consensus regarding this threshold value, nor has it been subject to a political process and can therefore be regarded as nothing more than a tentative suggestion.

Clinical evaluation - Methods

Literature search

Research librarian Ingrid Harboe planned and executed all systematic searches in collaboration with the project group. The strategy included both subject headings (MeSH, Emtree) and text words. Searches were limited to systematic reviews (SR) and controlled studies, both in the time period from 1995 to the date for the search. The reason for choosing 1995 as the starting point was that erythropoietin was introduced about that time (for more information about erythropoietin see Glossary and abbreviations). The searches for SRs and controlled studies were performed separately. The complete search strategies are listed in appendix 1.

We searched the following databases:

- The Cochrane Library; CDSR, DARE, Central, HTA, NHS EED
- Centre for Reviews and Dissemination (CRD); DARE, HTA, NHS EED
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to present
- EMBASE (Ovid) 1980 to present

We checked the reference lists in systematic reviews that we reviewed in full text, and performed manual searches in the following websites:
INAHTA (International Network of Agencies for Health Technology Assessment), **Clinical Evidence, ISI Web of Knowledge, NHS Evidence, AHRQ** (Agency for Healthcare Research and Quality's), **SBU** (Swedish Council on Health Technology Assessment)**, Dacehta, Finohta/ THL** (National Institute for Health and Welfare), **CADTH** *(*Canadian Agency for Drugs and Technologies in Health*),* **AHTA** *(*Adelaide Health Technology Assessment *),* **NIHR** (National Institute for Health Research), and **NICE** (National Institute for Health and Care Excellence).

Inclusion criteria

Population	Patients above 18 years with end-stage renal failure, independent of comorbidity, who need dialysis treatment, either as life-time treatment or while waiting for kidney transplantation

Interventions	Hemodialysis carried out in hospital Self-care hemodialysis carried out in hospital Hemodialysis carried out in satellite unit Hemodialysis carried out in the patient's home Peritoneal dialysis (continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD)) carried out at home after training in hospital
Comparator:	Dependent on available data we intended to compare all interventions with the alternative interventions.
Outcomes:	Mortality Quality of life (QoL) Complications that require special measures (*i.e.* hospitalisation, antibiotic treatment)
Study design:	Systematic reviews Randomized controlled trials Controlled observational studies
Languages:	No limitations in languages during the search, but we only included articles in English, articles with English abstract or articles in Scandinavian.

Selection of articles

Two reviewers independently inspected all citations generated by the search in order to identify potentially relevant articles based on title and/or abstract. Full text publications were obtained for articles appearing to meet the inclusion criteria or in cases where sufficient information was not available to make a decision. Two persons independently assessed whether the article was relevant or not according to our list of inclusion criteria. Disagreements were resolved by discussion or by consulting a third reviewer.

Articles meeting the pre-defined inclusion criteria were assessed for risk of bias (11). All assessments were performed and agreed upon by two researchers.

In addition to assessing risk of bias, we also performed a close inspection of baseline characteristics in the different treatment groups included in the studies. To be certain that the estimates of efficacy or safety reflected the delivered treatments, and not different prognostic features of the patients, we examined the baseline data of patients included in the studies. If differences in comorbidity between groups were reported or detected by our own analysis; or if no description of the patients comorbidity were reported, descriptive information about the study will only be presented in an Appendix. If however the article provided analyses that adjusted for this difference, the study will be included in our analyses and our assessments. This

means that the studies presented in the Appendix had either no comorbidity data reported or had adjustments that did not fulfil our study aim.

Data analysis

One reviewer extracted data from the included articles and another reviewer checked these results for accuracy. We extracted data as they were presented in the included publications. When data were presented in several ways, we chose to report data in our preferred order: hazard ratio (HR), relative risk (RR) and odds ratio (OR) with 95 % confidence intervals (CI). Where both unadjusted and adjusted data were available, we preferred adjusted data if adjustments seemed reasonable. When possible we performed meta-analyses using a random effects model. Forest plots are presented in the results section. Sometimes, when we found it helpful, we also presented outcome data from a single study in forest plots.

In cases where both events and patients at risk were available from the publications for all studies for a specific outcome, RRs were calculated using the Mantel-Haenzel approach in Review Manager. When the data regarding the same outcome were reported in different ways in the included publications, we re-calculated to log risk ratios and standard error, and the common RR was calculated using inverse variance in Review Manager. Footnotes in the forest plots provide details about the original data.

Grading the quality of evidence

Two persons assessed the overall documentation for each outcome by using GRADE (Grading of Recommendations, Assessment, Development and Evaluation, www.gradeworkinggroup.org). In the GRADE system outcome documentation from observational studies starts at low quality and outcome documentation from randomized controlled trials starts at high. The method involves an evaluation of study type, study quality/risk of bias, consistency between trials, directness (how similar the population, intervention, and outcomes are between the trials and the objectives of this report) and precision of the estimates. For the observational studies it is possible to rate up the quality of evidence. The three primary reasons for rating up are: 1) a large magnitude of effect exists; 2) there is a dose-response gradient, and 3) all plausible confounders or other biases increase our confidence in the estimated effect. Finally the overall quality will be categorized as high, moderate, low or very low.

GRADE gives the following definition of the different classes of evidence:

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Clinical evaluation - Results

Result of the literature search

The literature searches were done in May 2012, and updated in August 2013, see Appendix 1 for details. We searched both for systematic reviews/HTAs and controlled studies. We identified 109 systematic reviews/HTAs of which 24 were reviewed in full text. None fulfilled our inclusion criteria upon closer inspection. We identified 4346 controlled studies, of which 157 titles were found to be potentially relevant and full text copies were reviewed. Of those we included 33 studies. We also performed a manual search in the reference lists of included systematic reviews and websites of sister HTA agencies (the website searches were done in April 2012), identifying two controlled studies. Finally, 35 publications met our pre-specified inclusion criteria. A full list of the excluded studies and the reason for the exclusion is given in Appendix 2.

However, 17 of the included 35 publications either reported insufficient details or lacked data about patient comorbidities. Accordingly we only present descriptive information for these studies in Appendix 3. Ultimately, 18 publications constitute the documentation and are summarized in this report. These publications report results from two randomized controlled studies and 17 observational studies (Figure 3).

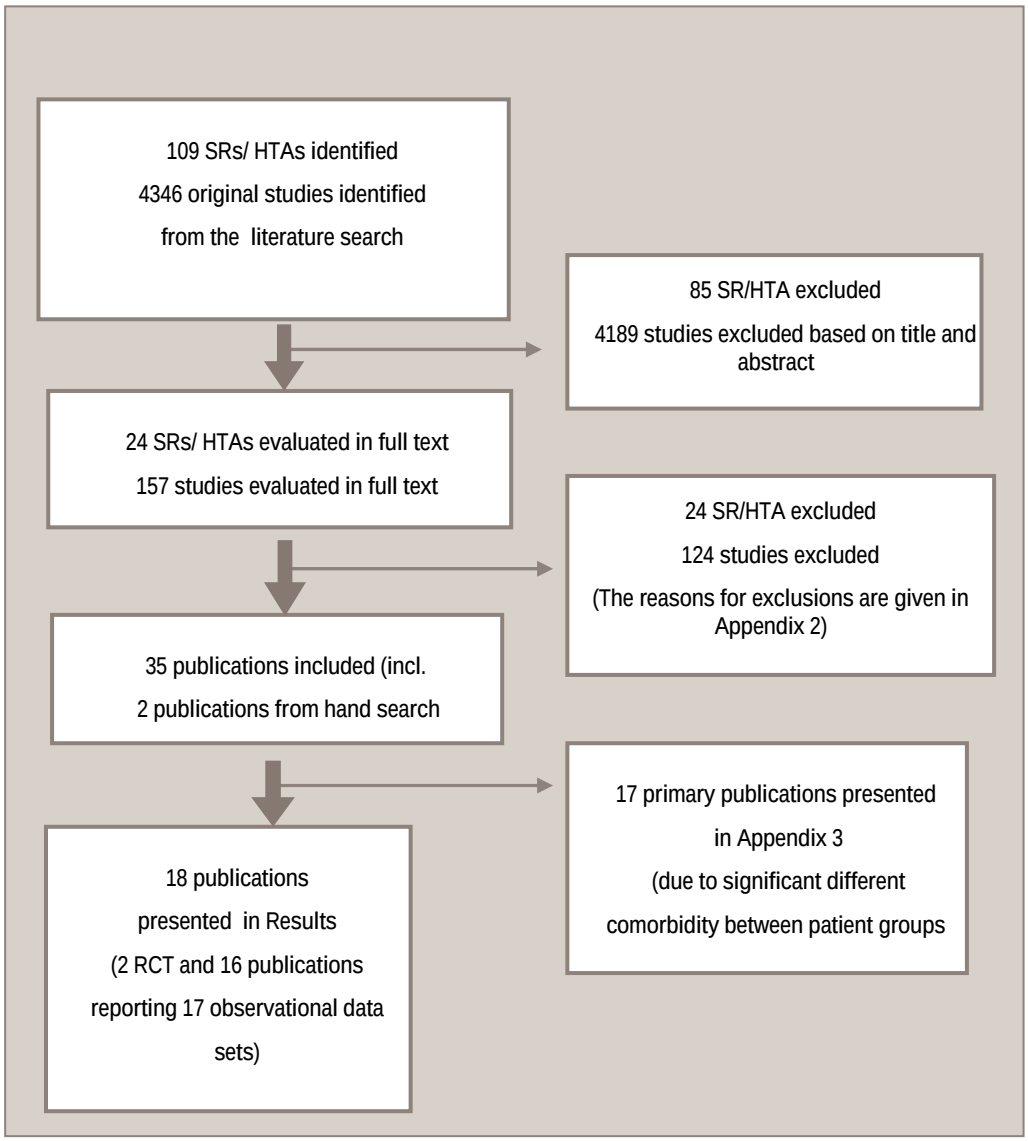


Figure 3 *Flowchart of identification of documentation.*

Ongoing studies

In August 2013 we searched WHO International Clinical Trials Registry Platform Search Portal (ICTRP) and Clinical Trials.gov to search for ongoing studies. We found no relevant studies (Appendix 1).

Description of the studies included in our assessment

Study design

Of the 18 publications two were RCTs and 16 were publications with data from 17 observational studies (12-28). The 17 observational studies included ten retrospective cohort studies, three prospective cohort studies and four cross-sectional studies. The articles were published between 1999 to 2012 with study periods from 1994 to 2008. The studies were performed in the USA (5), The Netherlands (2), Spain (2), Canada (2) and Denmark (1), England and Wales (1), France (1), Greece (1), China (1), Mexico (1), Malaysia (1) and Singapore (1). The two RCTs included 34 and 38 patients respectively, while patient totals ranged from 28 to 1238 in the observational studies. Duration of follow-up was 4-86 months.

Population

All patients included were above 18 years of age and had end stage renal disease requiring dialysis. The mean age of the patients in the studies ranged from 41 to 79, and the percent males in the studies ranged from 26 to 73 % (13 of the 19 studies had more than 50 % men). The compared patient groups in the studies we have used for outcome assessment had no significant differences in baseline comorbidity.

Intervention/controls

Of 21 possible comparisons, only six had data usable for our analyses. Figure 2 below shows the possible comparisons and outcomes reported for the specific comparisons. Outcomes in bold are those where the patient groups had no significant difference in comorbidity, or with analysis that adjusted for this. Those are presented in the following pages.
Outcomes in brackets are from studies that either had no comorbidity data reported, or had adjustments that did not fulfil our study aim. Information from such studies is only presented descriptively in the Appendix 3.

The comparison with most data was peritoneal dialysis (PD) versus hemodialysis in hospital (HD hospital). Peritoneal dialysis was done at home. Peritoneal dialysis can be of two types, either as continuous ambulatory peritoneal dialysis (CAPD) or as automated peritoneal dialysis. When we compared PD versus HD we did not specify if the peritoneal dialysis were given as CAPD or APD. The reason for this is that most of these studies did not specify the type of peritoneal dialysis used. However, two studies (14;24) had as aim to compare APD versus CAPD.
The frequency of dialysis for hemodialysis varied between the studies from 3 times per week to 5-7 times per week.

	HD hospital	HD self care hospital	HD satellite	HD home	CAPD home	APD home	PD home
HD hospital							
HD self care hospital	No data						
HD satellite	Complications (1 study) QoL (1 study) [Mortality]	No data					
HD home	[Mortality]	No data	Mortality (3 studies) Complications (2 studies) [Mortality]				
CAPD home	No data	No data	No data	No data			
APD home	No data	No data	No data	No data	Mortality (1 study) Complications (2 studies) QoL (1 study) [Mortality, complications]		
PD home	Mortality (7 studies) Complications (4 studies) QoL (3 studies) [Mortality, Complication, QoL)]	No data	Mortality (1 study) Complications (2 studies) [Mortality, QoL]	Complications (1 study) QoL (1 study) [Mortality]	No data	No data	

Figure 4 *Site comparisons with documentation. [Outcomes in brackets are only presented in Appendix 3*]

HD=hemodialysis; PD= peritoneal dialysis; CAPD= continuous ambulatory peritoneal dialysis; APD=automated peritoneal dialysis.

QoL= quality of life

Outcomes

Mortality was reported in 11 of the studies we assessed. It was reported as events (12;13;24;26), hazard ratios (18;19;27), relative risk (17), Kaplan Meier survival (16) and percent survival (21). One publication gave no data, but only reported that there was no significant difference in mortality (25).

Complications that require special measures were reported in ten studies. Complications were reported as hospital days (12;16;20;22;25;26), hospital

admissions, including different reasons for admissions (12;13;16;18;20;22;25;28), infections, including different types of infections (14;16;24;26), cardiovascular events (16), cerebrovascular accidents (16) and septic arthritis (16). Complications were reported in different ways in the publications.

Quality of life was reported in five publications. The tools used were SF-36 (The Short Form (36) Health Survey) mental component (19;22;23;29), SF-36 physical component (19;22;23;29), KDQL (Kidney Disease Quality of Life) (15;22), EuroQoL (European Quality of Life) (22). Quality of life was measured as mean difference ± standard differences.

Risk of bias for the included publications

We assessed the risk of bias for the included RCTs to be unclear for Bro *et al.* 1999 (14) and high for Korevaar *et al.* 2003 (19). The reason for the high risk of bias for Korevaar was that the study was planned statistically to include 100 patients; however, it was stopped after three years due to recruiting problems (only 38 patients randomised). Bro because it was not described if the outcomes assments were blinded. We assessed all of the observational studies to have relative high risk of bias, mainly due to lack of randomization. Our asessments are shown in Table 1 below.

Table 1: *Risk of bias for the included publications*

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
RCTs							
Bro 1999 (14)	+	+	+	?	+	+	?
Korevaar 2003 (19)	+	+	+	+	+	+	-
Observational studies							
Vigneau 2000 (26)	-	-	+	+	+	?	?
Jager 2001 (17)	-	-	+	+	?	+	?
Roderick 2005 (22)	-	-	+	+	+	+	?
Aslam 2006 (13)	-	-	+	+	+	+	?
Fong 2007 (15)	-	-	?	+	+	-	?

Zhang 2007 (29)	-	-	?	+	+	+	?
Andrikos 2008 (12)	-	-	+	+	+	+	?
Kumar 2008 (20)	-	-	+	?	-	-	?
Lee 2008 (21)	-	-	+	+	-	+	?
Sanchez 2008 (24)	-	-	+	?	?	+	?
Ganeshadeva 2009 (16)	-	-	+	+	+	+	?
Johansen 2009 (18)	-	-	+	+	?	+	?
Ruiz Retana 2009 (23)	-	-	?	?	?	?	?
Verdalles 2010 (25)	-	-	+	+	+	?	+
Williams 2011 (28)	-	-	+	+	+	+	?
Weinhandl 2012 (27)	-	-	+	+	?	+	?

+; Low risk, -; High risk, and ?; Unclear risk of systematic error.

The efficacy results for each comparison will be presented separately (see below).

PD home versus HD hospital

Description of the included studies

We included nine studies (12;16;17;19;21;23;25;26;29) for the comparison of patients receiving PD at home versus patients receiving HD in hospital. An overview of the studies is presented in Table 2. Details on patient characteristics at baseline can be seen in Appendix 4, Table I.

We report results for mortality, complications and quality of life. Seven of the eight studies reported mortality data, four studies reported data on complications and three studies reported data on quality of life.

Peritoneal dialysis was performed at home in all of the studies. Four studies specified the treatment as continuous ambulatory peritoneal dialysis (CAPD) (16;19;23;25).

Three additional studies had patient groups that were significant different in comorbidity. The studies had used adjusted analysis, but the adjustments used did not fulfil our study aim. Further information about these studies, and about seven studies that lacked comorbidity data altogether, is presented in Appendix 3.

Table 2: *The identified studies used in our assessment of PD home versus HD hospital*

Author year	Study type	Follow-up (months)	Country performed/ Number of participants	Outcomes	Risk of Bias
Korevaar 2003 (19)	RCT	60	Netherlands/ N=38	Mortality, QoL	High
Andrikos 2008 (12)	Retrospective cohort	Median 48.5 (6-60)	Greece/ N=94	Mortality Complication	High
Ganeshadeva 2009 (16)	Retrospective cohort	12	Malaysia /N=137	Mortality Complications	High
Jager 2001 (17)	Prospective cohort	Median 28 (4-44)	Netherlands/ N=250	Mortality	High
Lee 2008 (21)	Retrospective cohort	12	Singapore/ N=534	Mortality	High
Ruiz Retana 2009 (23)	Cross sectional		Spain/ N=93	QoL	High
Zhang 2007* (29)	Cross sectional		China/ N=1062	QoL	High
Verdalles 2010 (25)	Uncertain if retrospectie or prospective cohort	40±26	Spain/ N=139	Mortality Complications	High
Vigneau 2000 (26)	Retrospective cohort	14	France /N=28	Mortality Complications	High

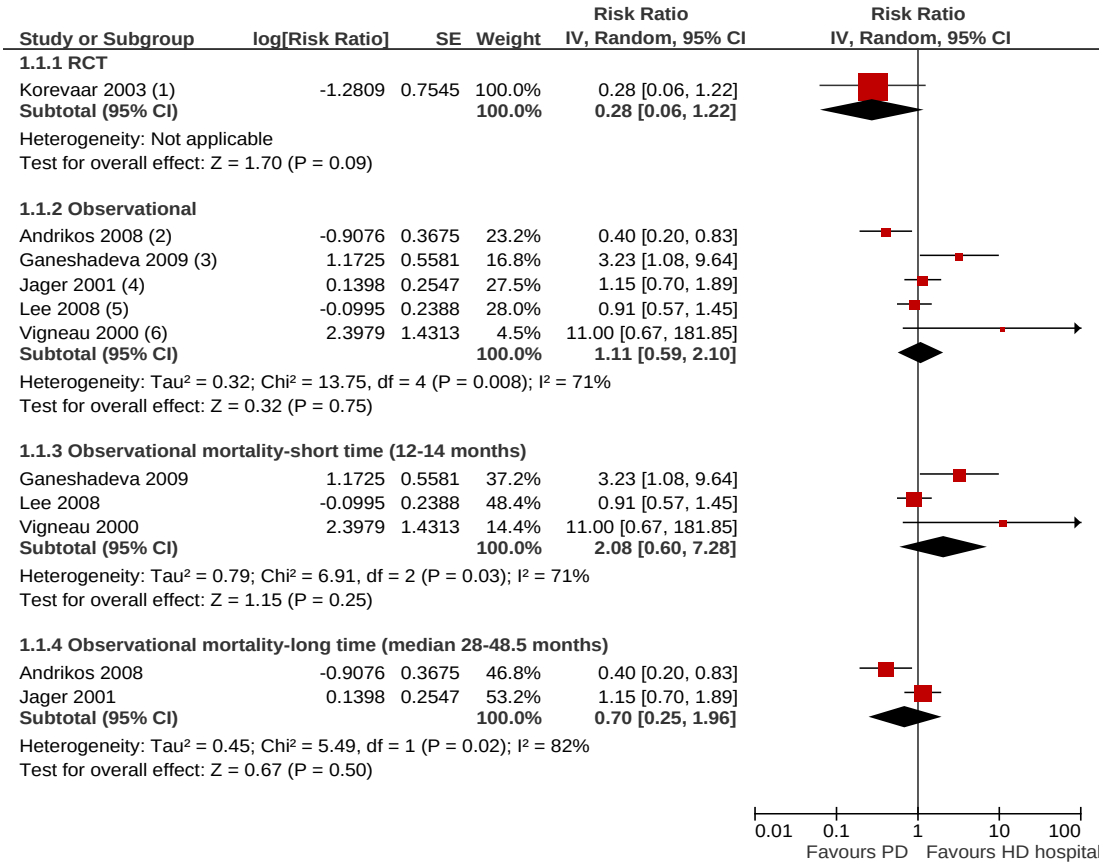
* Significant differences in comorbidity at baseline, but only adjusted analysis for quality of life.

Efficacy results for the comparison PD home versus HD hospital

Mortality

Seven studies reported mortality data (12;16;17;19;21;23;26). We found no significant difference in mortality between the patients receiving PD at home and patients receiving HD in hospital (Figure 5). The relative risk in the RCT was 0.28 (0.06 to 1.22) while a meta-analysis of observational studies resulted in RR 1.11 (0.59 to 2.10). One additional observational study also reported no significant difference in survival between the groups (25).

For the observational studies it was possible to do sensitivity analyses for different treatment durations. Neither showed a significant difference in mortality between the patient groups (Figure 5).



(1) Calculated log(Risk Ratio) from adjusted HR HDhospital vs PD
(2) log (Risk Ratio) calculated from reported events. ITT.Do not tell if adjusted or not
(3) log (Risk Ratio) calculated from Kaplan-Meier survival.ITT. Do not tell if adjusted or not
(4) log (Risk Ratio) calculated from reported RR. Adjusted. ITT?
(5) log (Risk Ratio) results calculated from survival data in percentage. ITT. Do not tell if adjusted or not
(6) log (Risk Ratio) calculated from reported events. ITT. Do not tell if adjusted or not

Figure 5 *Analyses of the mortality data from the RCT study and the observational studies respectively for the comparison PD home versus HD hospital.*

SE= Standard error. PD= peritoneal dialysis; HD= hemodialysis. ITT=Intention to treat.

Description of how we transformed the results to log relative risk and standard error is given in Appendix 5.

The quality of the evidence for mortality

For the RCT we evaluated the documentation for mortality for the comparison PD versus HD hospital to be of low quality (Table 3). For the observational studies we evaluated the total documentation for all the studies for mortality to be of very low quality (Table 3). The reasons for downgrading the quality for mortality are shown in the footnotes to Table 3.

Summary of findings for mortality for PD home versus HD Hospital

Table 3 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for mortality.

Table 3: *Summary of Findings Table for mortality for PD home versus HD hospital*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk HD hospital	Corresponding risk PD			
Mortality-RCT (Korevaar) Follow-up: 60 months	500 per 1000	140 per 1000 (30 to 610)	RR 0.28 (0.06 to 1.22)	38 (1 study)	⊕⊕⊖⊖ low[1,2,3,4]
Mortality – Observational Studies. All studies Follow-up: 4-60 months	144 per 1000[5]	160 per 1000 (85 to 302)	RR 1.11 (0.59 to 2.10)	793 (5 studies[7])	⊕⊖⊖⊖ very low[3,4,6]
Mortality – Observational studies-short term Follow-up: 12-14 months	116 per 1000	241 per 1000 (70 to 844)	RR 2.08 (0.6 to 7.28)	699 (3 studies)	⊕⊖⊖⊖ very low[3,4]
Mortality – Observational studies-long term Follow-up: median 28-48.5 months	413 per 1000[8]	289 per 1000 (103 to 809)	RR 0.70 (0.25 to 1.96)	94 (2 studies)	⊕⊖⊖⊖ very low[3,4]

[1] The study was planned/powered to 100 patients. Study stopped after 38 patients due to inclusion problems

[2] Only one study. Unclear reproducibility

[3] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>),

[4] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%

[5] Events taken from 4 of the 5 studies (Andrikos, Ganeshadeva, Lee, Vigneau)

[6] Unexplained heterogeneity

[7] One more study reported mortality, but only as no significant difference.

[8] Event numbers only available from Adrikos (Jager had no numbers).

HD= hemodialysis; PD= peritoneal dialysis.

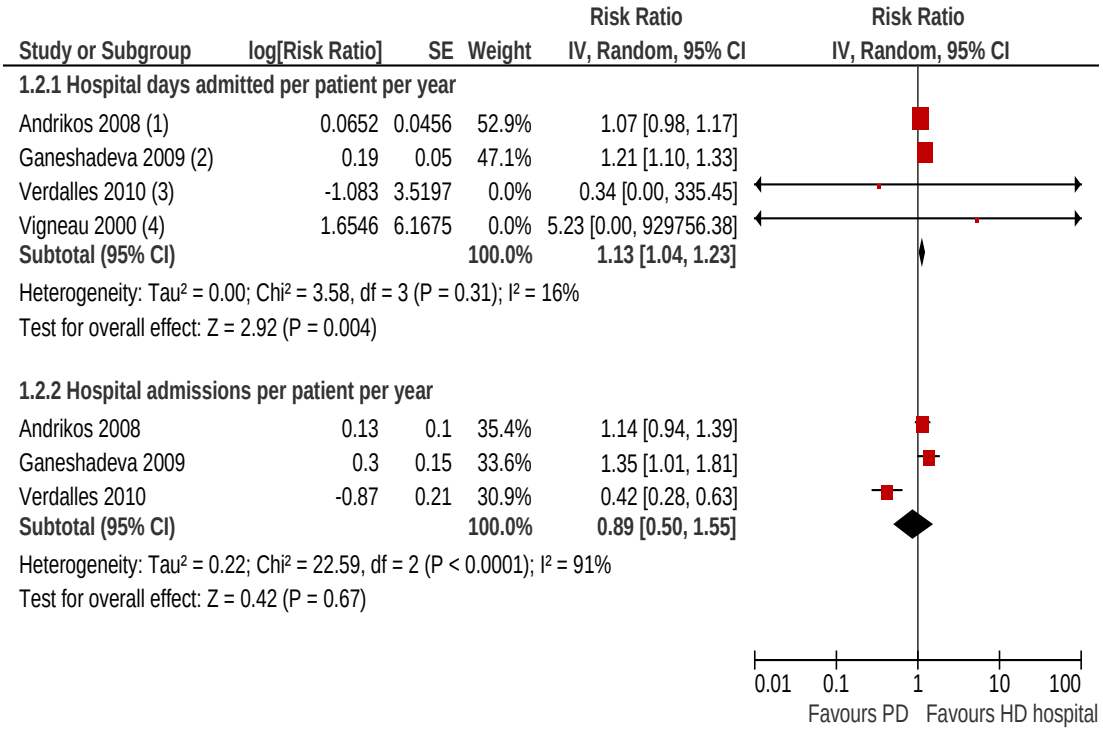
For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

The analyses did not find any significant differences in mortality between the patients in the PD and the HD hospital groups. The result are based on an RCT for which we assessed the mortality documentation quality to be low, and a meta-analysis of five observational studies for which we assessed the mortality documentation to be very low. Whether the results are due to poor study designs or true observations are for further studies to elucidate.

Complications that require special measures

Four studies reported results on complications that require special measures. Complications were reported as hospital days (12;16;25;26) or as hospital admissions (12;16;25). Forest plots for these outcomes are presented in Figure 6. Patients in the HD hospital group had significantly fewer hospital days admitted per patient per year than in the PD group: RR 1.13 (1.04 to 1.23); whereas there was no significant difference between the groups for hospital admissions per patient per year; RR 0.89 (0.50-1.55).



(1) log (RR) from days/patient/year. ITT. Do not tell if adjusted or not

(2) Log (RR) from days/patient-months at risk. ITT.Do not tell if adjusted or not

(3) log (RR) from days/year. ITT. Do not tell if adjusted or not.

(4) log (RR) from days hospitalised/months at risk. ITT. Do not tell if adjusted or not.

Figure 6 *Forest plot of hospital days and hospital admissions per patients per year respectively for the observational studies for the comparison PD versus HD hospital*

SE= standard error; HD= hemodialysis; PD= peritoneal dialysis. ITT= intention to treat.

Two of the studies (16;26) reported additional complications for the comparison PD home vs HD hospital (Table 4). However, with no outcomes in common, meta-analyses were not feasible. The analyses showed significant difference between the groups in favour of the PD patients for cardiovascular events including arrhythmias (RR 0.17 (0.07- 0.38), p<0.0001) and for all acute coronary syndromes (RR 0.03 (0 - 0.54), p=0.02). For dialysis modality related infections there was a significant difference in favour of the HD hospital patients; RR 137.36 (8.46-2228.93), p=0.0005. For all of the other reported complications there were no significant difference between the patient groups.

The quality of the evidence for complications

We evaluated the documentation for hospital days admitted per patient per year to be low. All of the other outcomes for complications were evaluated as very low (Table 4). The reasons for downgrading the quality for mortality are shown in the footnotes to Table 4.

Summary of findings for complications that require special measures for PD home versus HD hospital

Table 4 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for the complications

Table 4: *Summary of Findings Table for the reported complications for PD home versus HD hospital*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk HD hospital	Corresponding risk PD			
Hospital days per patient per year Follow-up: 6-60 months	Do not have total events		RR 1.13 (1.04 to 1.23)	398 (4 studies)	⊕⊕⊖⊖ low
Hospital admissions per patient per year Follow-up: 6-60 months	Do not have total events		RR 0.89 (0.5 to 1.55)	370 (3 studies)	⊕⊖⊖⊖ very low[1,2]
Infections (Vigneau 2000) Follow-up: mean 14 months	286 per 1000	644 per 1000 (257 to 1000)	RR 2.25 (0.9 to 5.62)	28 (1 study)	⊕⊖⊖⊖ very low[1,3,4]

Cardiovascular events including arrhytmias (Ganeshadeva 2009) Follow-up: 12 months	Background risk of CV events in HD patients in hospital is 1 per 68,4 patient month at risk	RR 0.17 (0.07 to 0.38)	137 (1 study)	⨁⊖⊖⊖ very low[3,4]	
All acute coronary syndromes (Ganeshadeva 2009) Follow-up: 12 months	Background risk of all acute coronary syndromes in HD patients in hospital is 1 per 177,6 patient month at risk	RR 0.03 (0 to 0.54)	137 (1 study)	⨁⊖⊖⊖ very low[3,4]	-
Cerebrovascular accidents (infarct and hemorrhages) (Ganeshadeva 2009) Follow-up: 12 months	Background risk of cerebrovascular accidents in HD patients in hospital is 1 per 880,0 patient month at risk	RR 0.8 (0.16 to 3.86)	137 (1 study)	⨁⊖⊖⊖ very low[1,3,4]	
Dialysis modality access dysfunctions (Ganeshadeva 2009) Follow-up: 1 2 months	Background risk of dialysis modality access dysfunction in HD patients in hospital is 1 per 55,5 patient month at risk	RR 0.96 (0.66 to 1.39)	137 (1 study)	⨁⊖⊖⊖ very low[1,3,4]	
Dialysis modality related infections (Ganeshadeva 2009) Follow-up: 1 2 months	Background risk of dialysis modality related infections in HD patients in hospital is 1 per 125 patient month at risk	RR 137.36 (8.46 to 2228.93)	137 (1 study)	⨁⊖⊖⊖ very low[3,4]	
Pneumonia (Ganeshadeva 2009) Follow-up: 12 months	Background risk of pneumonia in HD patients in hospital is 1 per 444 patient month at risk	RR 2.16 (0.92 to 5.09)	137 (1 study)	⨁⊖⊖⊖ very low[1,3,4]	
Septic Arthritis (Ganeshadeva 2009) Follow-up: 12 months	Background risk of septic arthritis in HD patients in hospital is 1 per 444 patient month at risk	RR 1.2 (0.45 to 3.21)	137 (1 study)	⨁⊖⊖⊖ very low[1,3,4]	

[1] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%

[2] Unexplained heterogeneity

[3] Only one study. Unclear reproducibility

[4]Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>

HD= hemodialysis; PD= peritoneal dialysis; RR= relative risk.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

We found significant fewer hospital days per patient per year in the HD hospital group than in the PD group. The results are based on documentation from four observational studies. We assessed the quality of the documentation to be low. This means that our confidence in the effect estimate is limited.

We found a significant difference in favour of the HD hospital patients for dialysis modality related infections. The result is based on documentation from one observational study where we assessed the quality of the documentation to be very low. This means that we have very little confidence in the effect estimate.

There were significantly fewer PD patients than HD hospital patients that developed cardio-vascular events including arrhythmias and acute coronary syndromes. The result is based on documentation from one observational study (the same as above) where we assessed the quality of the documentation to be very low. This means that we have very little confidence in the effect estimate.

For all of the other reported complications (hospital admissions, infections, cerebrovascular accidents (infarct and hemorrhages), dialysis modality access dysfunctions, pneumonia and septic arthritis) we found no significant difference between the patient groups. The results for hospital admissions per patients per year are based on documentation from three observational studies, whereas the documentation for all the other outcomes came from one observational study. For all these outcomes we assessed the documentation to be very low. This means that we have very little confidence in the effect estimate.

Quality of life

Three studies reported on quality of life (19;23;29), one RCT (19) and two observational studies. Quality of life was measured as mean quality-adjusted life years (QALY) or the physical and mental components of the SF-36. All were measured as mean difference ±SD. The different outcomes, length of the studies and the results of the comparison for each outcome are shown in Table 5 for two of the studies (19;23). Neither of the two showed significant differences between the groups. The third study (29) could not be included in our analysis since it only reported p-values, 0.098 and 0.009 (higher in the PD patients than in the HD hospital patients) respectively for physical functioning and mental health.

The quality of the evidence for quality of life

For the RCT we evaluated the documentation for quality of life (QALY scores) to be low. For the cross-sectional study the documentation for quality of life (SF-36 physical and mental component) was evaluated to be very low (Table 5). The reasons for downgrading the quality for quality of life are shown in the footnotes to table 5.

Summary of findings for quality of life the PD home versus HD hospital

Table 5 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for quality of life.

Table 5: *Summary of Findings Table for quality of life for PD home versus HD hospital*

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk HD hospital	Corresponding risk PD	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
Quality of life - RCT EuroQoL VAS score adjusted (Korevaar 2003) Follow-up: 24 months	The mean Quality of life - RCT QALY score adjusted in the intervention groups was 0.05 lower (0.15 lower to 0.05 higher)			38 (1 study)	⊕⊕⊖⊖ low[1,2]
Quality of life – Observational SF-36 Physical (Ruiz Retana 2009) Cross sectional	The mean Quality of life - Observational SF-36 Physical in the intervention groups was 1.10 higher (3.15 lower to 5.35 higher)			93 (1 study)	⊕⊖⊖⊖ very low[2]
Quality of life - Observational SF-36 mental (Ruiz Retana 2009) Cross sectional	The mean Quality of life - Observational SF-36 mental in the intervention groups was 2.60 lower (10.69 lower to 5.49 higher)			93 (1 study)	⊕⊖⊖⊖ very low[2]

[1] The study was planned/powered to 100 patients. Study stopped after 38 patients due to inclusion problems

[2] Only one study. Unclear reproducibility

HD= hemodialysis; PD= peritoneal dialysis; RR= relative risk.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

The results for quality of life were based upon data from one RCT and two observational studies (one of those gave only p-values). Neither the RCT nor the observa-

tional study that presented data showed significant differences in quality of life between the groups. We evaluated the documentation for quality of life from the RCT to be of low quality. This was a small study with 38 patients that was stopped prematurely due to recruiting problems. This means that our confidence in the effect estimate is limited. The results from the cross-sectional study were based on documentation with very low quality and hence we have very little confidence in the effect estimate. The third study (29)- that was not included in our analysis since it only reported p-values -showed significant higher scores for mental health in the PD patients than in the HD hospital patients. Due to lack of data we were not able to perform GRADE for this outcome.

HD satellite versus HD hospital

Description of the included studies

Only one study (22) met our inclusion criteria and reported comparable treatment groups for the comparison of HD delivered in a satellite unit compared to HD delivered in a hospital. An overview of the study is presented in Table 6. Details on patient characteristics at baseline can be seen in Appendix 4, Table II.

Two additional studies lacked information about comorbidity. Information related to these studies is presented in Appendix 3.

Table 6: *The identified study used in our assessment of HD satellite versus HD hospital*

Author year	Study type	Follow-up time (months)	Country performed/ Number of participants	Outcomes	Risk of Bias
Roderick 2005 (22)	Cross sectional	12 months	England and Wales/736	Complications Quality of life	High

Efficacy of HD satellite versus HD hospital

Mortality

For this comparison there was no mortality data.

Complications that require special measures

Roderick *et al.* 2005 (22) reported data regarding five different complications. They reported a significant difference in favour of HD satellite for patients hospitalised, RR 0.80 (0.67-0.95), p= 0.01. We further analysed the reported documentation and found a significant difference also for infections, again in favour of HD satellite; RR 0.55 (0.32-0.96), p=0.03. For hospitalisation due to cardiac or vascular causes we analysed the reported data and found a borderline significant difference in favour of HD satellite, RR 0.53 (0.28 to 1.01), p=0.05. Results are shown in Table 7. The forest plot showing our analyses can be seen in Appendix 7, Figure I. The length of stay in

hospital was reported as mean±SD per patients. There was no significant difference between the groups for this outcome; SD -1.10 (-2.60 to 0.40), p=0.15 (Table 7).

The quality of the evidence for complications that require special measures
We evaluated the documentation for all of the complication outcomes as very low. The different outcomes and the reasons for downgrading the quality for those are shown in the footnotes to Table 7.

Summary of findings for complications that require special measures for HD satellite versus HD hospital

Table 7 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for the reported complications.

Table 7: *Summary of Findings Table for complications for HD satellite versus HD hospital*

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk HD hospital	Corresponding risk HD satellite	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
Patients hospitalized Follow-up: 1 years	447 per 1000	358 per 1000 (299 to 425)	RR 0.8 (0.67 to 0.95)	736 (1 study)	⊕⊖⊖⊖ very low[1]
Access related hospitalisation Follow-up: 1 years	178 per 1000	157 per 1000 (114 to 217)	RR 0.88 (0.64 to 1.22)	736 (1 study)	⊕⊖⊖⊖ very low[1,2,3]
Access formation hospitalisation Follow-up: 1 years	123 per 1000	102 per 1000 (68 to 153)	RR 0.83 (0.55 to 1.24)	736 (1 study)	⊕⊖⊖⊖ very low[1,2,3]
Cardiac or vascular hospitalisation Follow-up: 1 years	67 per 1000	36 per 1000 (19 to 68)	RR 0.53 (0.28 to 1.01)	736 (1 study)	⊕⊖⊖⊖ very low[1,2,3]
Infections (not access related) hospitalisation Follow-up: 1 years	88 per 1000	48 per 1000 (28 to 84)	RR 0.55 (0.32 to 0.96)	736 (1 study)	⊕⊖⊖⊖ very low[1,2]
Length of stay in hospital (days/per patient) Follow-up: mean 1 years	The mean length of stay in hospital (days/per patient) in the control groups was 4.7 days	The mean length of stay in hospital (days/per patient) in the intervention groups was 1.10 lower (2.6 lower to 0.4 higher)		736 (1 study)	⊕⊖⊖⊖ very low[1,3]

[1] Only one study. Unclear reproducibility

[2] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>)

[3] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

HD= hemodialysis.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?
All the results for complications were based upon data from one observational study. There were significant fewer patients hospitalised and fewer infections in the HD satellite group than in the HD hospital group. For hospitalisation due to cardiac or vascular causes there was a borderline significant difference in favour of HD satellite group. There was no significant difference between the groups for days per patient in hospital.
We assessed all of the documentation for the complications to be of very low quality, hence we have very little confidence in these effect estimates.

Quality of life
Roderick *et al.* 2005 (22) measured quality of life using EQ-5D utilities, SF-36 physical and mental summary score) and by KDQL

KDQL was reported as pooled (combined) estimate of mean satisfaction score, the difference was 7.50 (1.33 to 13.67). The score was significantly higher in the HD satellite group. The number of patients included in any of the 11 items for KDQL varied from 70-334 for the satellite group and from 80-281 for the hospital group.
The SF-36 mental score was significant lower in the HD satellite group. Quality of life measured withSF-36 physical score and EQ-5D show no significant differences between the patient groups.
Results are presented in Table 8.

The quality of the evidence for quality of life
We evaluated the documentation for all of the quality of life outcomes as very low. The different outcomes and the reasons for downgrading the quality for those are shown in the footnotes to Table 8.

Summary of findings for quality of life for HD satellite versus HD hospital
Table 8 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for quality of life.

Table 8: *Summary of Findings Table for quality of life for HD satellite versus HD hospital*

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk HD hospital	Corresponding risk HD satellite	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
Quality of life - EQ-5D utilities off dialysis EQ VAS scores	The mean Quality of life - EQ-5D utilities off dialysis in the intervention groups was 0.00 higher (0.05 lower to 0.05 higher)			583 (1 study)	⊕⊖⊖⊖ very low[1]
Quality of life - SF-36 physical score	The mean Quality of life - SF-36 physical score in the intervention groups was 0.02 higher (2.11 lower to 2.15 higher)			435 (1 study)	⊕⊖⊖⊖ very low[1]
Quality of life - SF-36 mental score	The mean Quality of life - SF-36 mental score in the intervention groups was 4.39 lower (6.58 to 2.2 lower).			435 (1 study)	⊕⊖⊖⊖ very low[1]
Quality of life - KDQOL	The mean Quality of life - KDQOL in the intervention groups was 7.5 higher (1.33 to 13.67 higher).			150 (sexual function) 611(burden of kidney disease) (1 study)	⊕⊖⊖⊖ very low[1]

[1] Only one study. Unclear reproducibility

HD= hemodialysis; PD= peritoneal dialysis; RR= relative risk.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

All the results for quality of life were based upon data from one observational study. The score for KDQL was significant higher in the HD satellite group than in the HD hospital group. Whereas the SF-36 mental score was significant lower in the HD satellite group than in the HD hospital group. Quality of life measured with SF-36 physical score and EQ-5D show no significant differences between the patient groups. We assessed all of the documentation for quality of life to be of very low quality. This means that we have very little confidence in these effect estimates.

PD home versus HD satellite

Description of the included studies

Two studies (13;28) met our inclusion criteria and reported comparable treatment groups for the comparison of PD performed at home compared to HD delivered in a satellite unit. An overview of the studies is presented in Table 9. Details on patient characteristics at baseline can be seen in Appendix 4, Table III.

Two additional studies had patient groups with significant differenence in comorbidity. One of these had no adjusted analysis and the other had used adjustments that did not fulfil our study aim. Further information about these

studies, and about one study that lacked comorbidity data altogether, is presented in Appendix 3.

Table 9 *The identified studies used in our assessment of PD home versus HD satellite*

Author year	Study type	Follow-up time (months)	Country performed/ Number of participants	Outcomes	Risk of Bias
Aslam 2006 (13)	Prospective cohort	15-18	USA/181	Mortality Complications	High
Williams 2011 (28)	Retrospective Cohort	23-27.5	Canada/168	Complications	High

Efficacy of PD home versus HD satellite

Mortality

Only one study reported on mortality (13). The analysis showed a significant difference in favour of the patients in the PD group; RR 0.41 (0.19-0.87), p=0.02 (Figure 7).

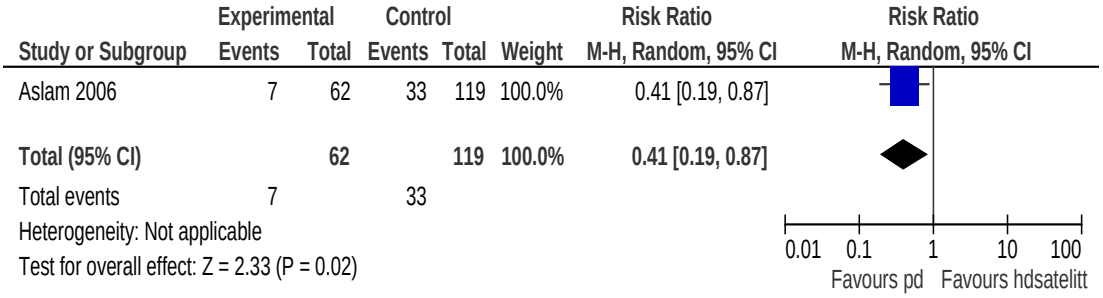


Figure 7 *Forest plot showing mortality for PD home versus HD satellite*

The analysis was adjusted.

HD= hemodialysis; PD= peritoneal dialysis.

The quality of the evidence for mortality

We assessed the documentation for mortality to be very low. The reasons for downgrading the quality are shown in the footnotes to Table 10.

Summary of findings for mortality for PD home versus HD satellite

Table 10 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for mortality.

Table 10: *Summary of Findings Table for mortality for PD home versus HD satellite*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk HD satellite	Corresponding risk PD			
Mortality Aslam Follow-up: 15-18 months	277 per 1000	114 per 1000 (53 to 241)	RR 0.41 (0.19 to 0.87)	181 (1 study)	⊕⊖⊖⊖ very low[1,2]

[1] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>),

[2] Only one study. Unclear reproducibility

HD= hemodialysis; PD= peritoneal dialysis.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

The result for mortality was based upon data from one observational study. We found a significant difference in favour of the patients in the PD group. However, we evaluated the documentation for mortality to be of very low quality, hence any estimate of effect is very uncertain.

Complications that require special measures

Both studies (13;28) included for this comparison reported data regarding complications. Forest plots for these outcomes are presented in Figure 8. The results was significant in favour of the PD patients for bacteremia-related hospitalisation, RR 0.08 (0.01 to 0.92), p=0.04. Hospitalisation due to infections, pneumonia and peritonitis showed no significant difference between the groups.

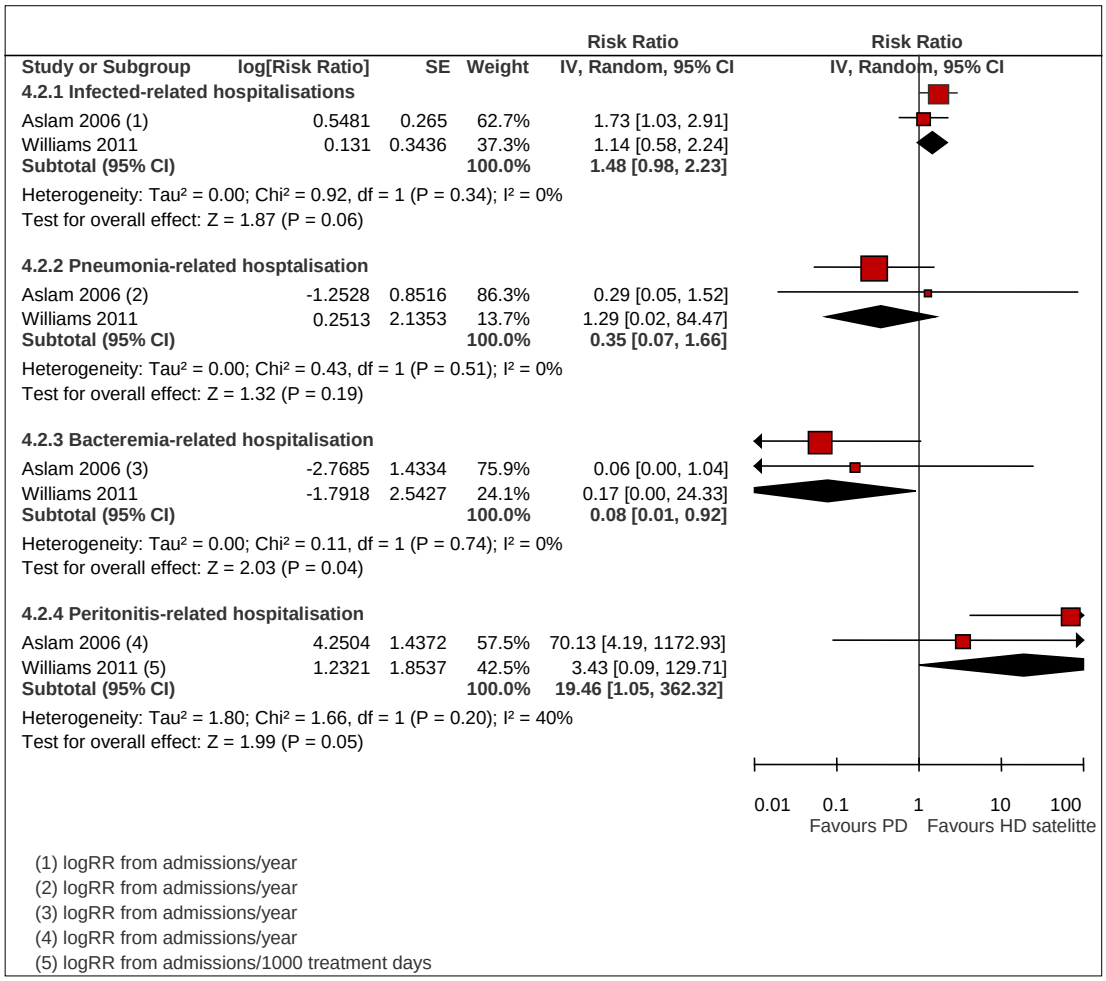


Figure 8 *Forest plot showing reasons for hospitalisation for PD home versus HD satellite*

The analyses for infected-related hospitalisation were adjusted. The analyses for pneumonia-, bacteremia- and peritonitis-related hospitalization were unadjusted.

HD= hemodialysis; PD= peritoneal dialysis.

Description of how we transformed the results to log relative risk and standard error is given in Appendix 5.

The quality of the evidence for complications that require special measures

We assessed the documentation for hospitalisation due to infections, pneumonia, bacteremia and peritonitis to be very low. The reasons for downgrading the quality are shown in the footnotes to Table 11.

Summary of findings for complications that require special measures for PD home versus HD satellite

Table 11 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for complications.

Table 11: *Summary of Findings Table for complications for PD home versus HD satellite*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk HD satellite	Corresponding risk PD			
Infection related hospitalisations Aslam ; Williams Follow-up: 15-27.5 months	175 per 1000[3]	259 per 1000 (172 to 390)	RR 1.48 (0.98 to 2.23)	168 (2 studies)	⊕⊖⊖⊖ very low[1,4]
Complications - Pneumonia Aslam; Williams Follow-up: 15-27.5 months	Do not have total events		RR 0.35 (0.07 to 1.66)	168 (2 studies)	⊕⊖⊖⊖ very low[1,2]
Complications – Bacteremia Aslam, Williams Follow-up: 15-27.5 months	Do not have total events		RR 0.08 (0.01 to 0.92)	168 (2 studies)	⊕⊖⊖⊖ very low[1]
Complications – Peritonitis Aslam, Williams Follow-up: 15-27.5 months	Do not have total events		RR 19.46 (1.05 to 362.32)	168 (2 studies)	⊕⊖⊖⊖ very low[1]

[1] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>),

[2] Only one study. Unclear reproducibility

HD= hemodialysis; PD= peritoneal dialysis.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

The results for hospitalisation due to different types of infections (infection, pneumonia, bacteremia, peritonitis) all came from two observational studies. We found a significant difference in favour of the PD patients for bacteremia-related hospitalisation. Hospitalisation due to infections, pneumonia and peritonitis showed no significant difference between the groups. However, we evaluated the documentation for all complication outcomes to be very low quality, hence any estimate of effect is very uncertain.

HD home versus HD satellite

Description of the included studies

Two publications (18;27) met our inclusion criteria and reported comparable treatment groups for the comparison of HD performed at home compared to HD delivered in a satellite unit. Johansen *et al.* 2009 (18) described two studies: nocturnal HD at home and short daily HD at home, each compared with its own matched group treated with conventional HD in a satellite unit. Weinhandl *et al.* 2012 (27) compared daily home HD with thrice-weekly HD in-center (satellite). An overview of the studies is presented in Table 12. Details on patient characteristics at baseline can be seen in Appendix 4, Table IV.

One additional studies lacked information about comorbidity. Information related to this study is presented in Appendix 3.

Table 12: The identified studies used in our assessment of HD home versus HD satellite

Author year	Study type	Follow-up time (months)	Country performed/ Number of participants	Outcomes	Risk of Bias
Johansen 2009 NHD* (18)	Retrospective cohort	Hdhome:56/ Hdsat:53	USA/1034	Mortality Complications	High
Johansen 2009 SDHD* (18)	Retrospective cohort	Hdhome:86/ Hdsat:81	USA/473	Mortality Complications	High
Weinhandl 2012 (27)	Retrospective cohort	Hdhome:22/ Hdsat:21	USA/11238	Mortality	High

*Johansen 2009 included two comparisons

Efficacy results for HD home versus HD satellite

Mortality

We performed a meta-analysis based on the reported mortality data in the included studies. We found no significant differences in mortality between the groups (Figure 9).

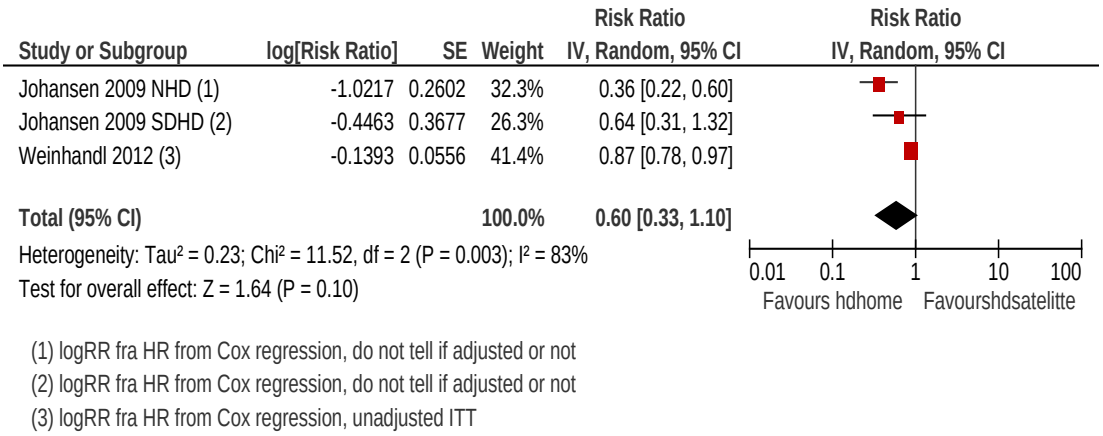


Figure 9 *Forest plot showing mortality for HD home versus HD satellite*

SE= standard error; HD= hemodialysis.

Description of how we transformed the results to log relative risk and standard error is given in Appendix 5.

The quality of the evidence for mortality

We have evaluated the documentation for mortality as low. That means that we found no reasons to downgrade.

Summary of findings for mortality for HD home versus HD satellite

Table 13 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for mortality.

Table 13: *Summary of Findings Table for mortality for HD home versus HD satellite*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk HD satelitte	Corresponding risk HD home			
Mortaltiy Johansen (2 studies in one publication) and Weinhandl Follow-up: 21-86 months	39 per 1000[1]	23 per 1000 (13 to 43)[1]	RR 0.60 (0.33 to 1.1)	12745 (3 studies)	⨁⨁⊖⊖ low

[1] Events measured as deaths /1000 patient-years

HD= hemodialysis.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

The results for mortality came from three observational studies. We found no significant differences in mortality between the groups, and we evaluated the documentation for mortality to have low quality. This means that our confidence in the effect estimate is limited.

Complications that require special measures

Only Johansen *et al.* 2009 (18) reported data regarding treatment complications. We present a forest plot of our meta-analysis for hospitalisation due to vascular access and congestive heart failure in Figure 10. Neither show significant difference between the groups.

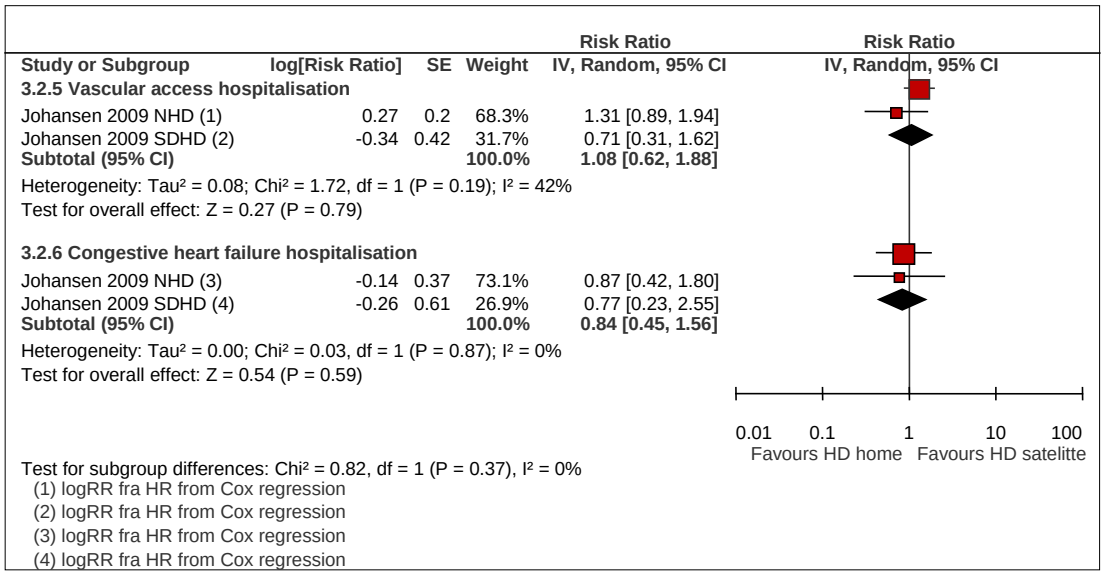


Figure 10 *Forest plot showing hospitalisation due to vascular access and congestive heart failure for HD home versus HD satellite*

SE= standard error; HD= hemodialysis.

Description of how we transformed the results to log relative risk and standard error is given in Appendix 5.

The quality of the evidence for complications that require special measures

We assessed the documentation for hospitalisation due to vascular access as well as due to congestive heart failure to be of very low quality. The reasons for downgrading the quality are shown in the footnotes to table 14.

Summary of findings for complications that require special measures for HD home versus HD satellite

Table 14 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for complications.

Table 14: *Summary of Findings Table for complications for HD home versus HD satellite*

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk HD satelitte	Corresponding risk HD home	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
Vascular access hospitalisation Johansen (2 studies in one publication) Follow-up: 53-86 months	No events reported (based upon hazard risk)		RR 1.08 (0.62 to 1.88)	1507 (2 studies)	⊕⊖⊖⊖ very low[1]
Congestive heart failure hospitalisation Johansen (2 comparisons in one study) Follow-up: 53-86 months	No events reported (based upon hazard risk)		RR 0.84 (0.45 to 1.56)	1507 (2 studies)	⊕⊖⊖⊖ very low[1]

[1] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

HD= hemodialysis.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

The results for hospitalisation due to vascular access as well as due to congestive heart failure were based on data from two observational studies. For both outcomes we found no significant differences between the groups and we evaluated the documentation to be of very low quality. Hence, we have very little confidence in the effect estimates.

HD home versus PD home

Description of the included studies

Two studies (15;20) met our inclusion criteria and reported comparable treatment groups for the comparison of HD performed at home compared to PD performed at

home. An overview of the studies is presented in Table 15. Details on patient characteristics at baseline can be seen in Appendix 4, Table V.

One additional study lacked information about comorbidity. Information related to this study is presented in Appendix 3.

Table 15: *The identified studies used in our assessment of HD home versus PD home*

Author year	Study type	Follow-up time (months)	Country performed/ Number of participants	Outcomes	Risk of Bias
Kumar 2008 (20)	Prospective cohort	20-22	USA/ 86	Complications	High
Fong 2007 (15)	Cross-sectional	Not applicable	Canada/ 93	Quality of life	High

Efficacy of HD home versus PD home

Mortality

No studies reported on mortality for this comparison.

Complications that require special measures

Kumar *et al.* (20) reported data on patients hospitalized and hospital days per patients due to different complications. The types of complications and the results are presented in Table 16.

The quality of the evidence for complications that require special measures

We assessed the documentation for patients hospitalized and hospital days per patients to be of very low quality. The reasons for downgrading the quality are shown in the footnotes to Table 16.

Summary of findings for complications that require special measures for HD home versus PD home

Table 16 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for complications.

Table 16: *Summary of Findings Table for complications for HD home versus PD home*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk PD	Corresponding risk HD home			
Patients admitted diagnosed with cardiac disease (angina, myocardial infarction, atrial fibrillation Kumar Follow-up: 20-22 months	125 per 1000	181 per 1000 (61 to 545)	RR 1.45 (0.49 to 4.36)	86 (1 study)	⊕⊖⊖⊖ very low[1,2,3]
Hospital days/patients for those diagnosed with cardiac disease (angina, myocardial infarction, atrial fibrillation) Kumar Follow-up: 20-22 months	641 per 1000	910 per 1000 (724 to 1000)	RR 1.42 (1.13 to 1.78)	86 (1 study)	⊕⊖⊖⊖ very low[2,3]
Patients admitted diagnosed with infectious disease (sepsis, cellulitis, abscess, urinary tract infection, pneumonia, gangrene) Kumar Follow-up: 20-22 months	188 per 1000	45 per 1000 (6 to 331)	RR 0.24 (0.03 to 1.76)	86 (1 study)	⊕⊖⊖⊖ very low[1,2,3]
Hospital days/patients for those diagnosed with infectious disease (sepsis, cellulitis, abscess, urinary tract infection, pneumonia, gangrene) Kumar Follow-up: 20-22 months	Not estimable. Events/number of patients for HD and PD: 6/22 and 125/64		RR 0 (0 to 0)[4]	86 (1 study)	⊕⊖⊖⊖ very low[2,3]
Patients admitted diagnosed with ESRD related congestive heart failure Kumar Follow-up: 20-22 months	62 per 1000	46 per 1000 (6 to 388)	RR 0.73 (0.09 to 6.16)	86 (1 study)	⊕⊖⊖⊖ very low[1,2,3]

Hospital days/ for those diagnosed with ESRD related congestive failure Kumar Follow-up: 20-22 months	266 per 1000	90 per 1000 (24 to 362)	RR 0.34 (0.09 to 1.36)	86 (1 study)	⊕⊖⊖⊖ very low[1,2]
Patients admitted diagnosed with ESRD related arterio-venous access complication (access infection, clotting, bleeding, endocarditis) Kumar Follow-up: 20-22 months	16 per 1000	233 per 1000 (29 to 1000)	RR 14.55 (1.8 to 117.8)	86 (1 study)	⊕⊖⊖⊖ very low[2]
Hospital days/patients for those diagnosed with ESRD related arterio-venous access complications (access infection, clotting, bleeding, endocarditis) Kumar Follow-up: 20-22 months	Not estimable. Events/number of patients for HD and PD: 53/22 and 1/64		RR (not estimable)	86 (1 study)	⊕⊖⊖⊖ very low[2]
Patients admitted diagnosed with peritonitis or tunnel infections Kumar Follow-up: 20-22 months	297 per 1000	21 per 1000 (0 to 342)	RR 0.07 (0 to 1.15)	86 (1 study)	⊕⊖⊖⊖ very low[2]
Hospital days/patients for those diagnosed with peritonitis or tunnel infections Kumar Follow-up: 20-22 months	Not estimable. Events/number of patients for HD and PD: 0/22 and 138/64		RR (not estimable)	86 (1 study)	⊕⊖⊖⊖ very low[2]

[1] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

[2] Total numbers of events less than 300

[3] Only one study Unclear reproducibility

[4] Not estimable

HD= hemodialysis; PD=peritonealdialysis

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

All the complication results (patients hospitalized and hospital days per patients) came from one observational study. We assessed the documentation for those outcomes to be of very low quality, hence we have very little confidence in the effect estimates.

Quality of life

Fong *et al.* 2007 (15) reported data for quality of life. They measured quality of life as KDQOL-SF, including physical and mental component summary. Neither show significant differences. The results are presented in Table 17.

The quality of the evidence for quality of life

We assessed the documentation for quality of life as very low. The reasons for downgrading the quality are shown in the footnotes to table 17.

Summary of findings for quality of life for HD home versus PD home

Table 17 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for quality of life.

Table 17: *Summary of Findings Table for quality of life for HD home versus PD home*

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk PD	Corresponding risk HD home	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Quality of life- KDCS Cross- sectional		The mean Quality of life- KDCS in the intervention groups was 6.90 higher (2.8 lower to 16.6 higher)		93 (1 study)	⊕⊖⊖⊖ very low[1,2]	
Physical component summary Cross-sectional		The mean Physical component summary in the intervention groups was 2.70 higher (3.02 lower to 8.42 higher)		93 (1 study)	⊕⊖⊖⊖ very low[1,23]	
Mental component summary Cross- sectional		The mean Mental component summary in the intervention groups was 1.60 higher (9.88 lower to 13.08 higher)		93 (1 study)	⊕⊖⊖⊖ very low[1,2]	

[1] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>),

[2] Only one study. Unclear reproducibility

HD= hemodialysis; PD=peritonealdialysis

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?
The results for quality of life came from one observational study. We found no significant differences between the groups in quality of life, and we evaluated all of the documentation for these outcomes to be of very low quality. Hence, we have very little confidence in the effect estimates.

Automated peritoneal dialysis at home (APD home) versus continuous ambulatory peritoneal dialysis at home (CAPD home)

Description of the included studies

Two studies (14;24) met our inclusion criteria and reported comparable treatment groups for the comparison of two different types of PD performed at home. An overview of the studies is presented in Table 18. Details on patient characteristics at baseline can be seen in Appendix 4, Table VI.

Three additional studies lacked information about comorbidity. Information related to these studies is presented in Appendix 3.

Table 18: *The identified studies used in our assessment of APD home versus CAPD home*

Author year	Study type	Follow-up time (months)	Country performed/ Number of participants	Outcomes	Risk of Bias
Bro 1999 (14)	RCT	6	Denmark/34	Complications Quality of life*	Unclear
Sanchez 2008 (24)	Retrospective cohort	12-36	Mexico/233	Mortality Complications	High

*No exact data, only from a figure and from text.

Efficacy results for APD home versus CAPD home

Mortality
Only Sanchez *et al.* 2008 (24) reported data regarding mortality. Patients survival at 1, 2 and 3 years was reported (Table 19). We calculated this as mortality and presented our results as a forest plot (Appendix 7, figure II). Estimates favour APD at all time points, this was significant after 1 (RR 0.48 (0.30-0.77), p=0.002) and 3 years (RR 0.69 (0.54-0.86), p= 0.001), and borderline significant after 2 years (RR 0.74 (0.55-1.00), p=0.05).

The quality of the evidence for mortality
We assessed the documentation for mortality to be very low. The reasons for downgrading the quality are shown in the footnotes to table 19.

Summary of findings for mortality for APD home versus CAPD home

Table 19 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for morality.

Table 19: *Summary of Findings Table for mortality for APD home versus CAPD satellite*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk CAPD	Corresponding risk APD			
Mortality 1 year Sanchez Follow-up: 1 years	381 per 1000	183 per 1000 (114 to 293)	RR 0.48 (0.3 to 0.77)	237 (1 study)	⊕⊖⊖⊖ very low[1,2]
Mortality 2 years Sanchez Follow-up: 2 years	511 per 1000	378 per 1000 (281 to 511)	RR 0.74 (0.55 to 1)	237 (1 study)	⊕⊖⊖⊖ very low[1,2]
Mortality 3 years Sanchez Follow-up: 3 years	583 per 1000	437 per 1000 (338 to 571)	RR 0.75 (0.58 to 0.98)	237 (1 study)	⊕⊖⊖⊖ very low[1,2]

[1] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>),

[2] Only one study. Unclear reproducibility

APD=automated peritoneal dialysis; CAPD=continuous ambulatory peritoneal dialysis; RR=relative risk

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

The documentation for mortality came one observational study, and we assessed the quality of this outcome to be very low. Hence, we have very little confidence in the effect estimate.

Complications that require special measures

Complications in the form of different infection types were reported in both the included studies (14;24). Peritonitis was reported in both the included RCT and the observational study. Due to different study designs these were not pooled in a meta-analysis. Results favoured APD, but this was only significant in the observational study (Table 20 and Appendix 7, figure III) The relative risks were 0.54 (0.06-5.24), p= 0.60 and 0.46 (0.34-0.63), p<0.00001) respectively for the RCT (14) and the observational study (24). Bro *et al.* 1999 (14) also reported on exit site infection (RR 1.08 (0.08-15.46), p=0.95) and tunnel infection (RR 3.23 (0.14-72.46), p=0.46). Neither showed statistically significant results (Table 20). The forest plot of our analyses can be seen in Appendix 7, figure IV.

The quality of the evidence for complications that require special measures

We assessed the documentation for peritonitis, exit-site infection and tunnel infection from the RCT (14) to be low. The documentation for peritonitis from the observational study was assessed by us as very low. The reasons for downgrading the quality are shown in the footnotes to table 20.

Summary of findings for complications that require special measures for APD home versus CAPD home

Table 20 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for complications.

Table 20: *Summary of Findings Table for complications for APD home versus CAPD satellite*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk CAPD	Corresponding risk APD			
RCT peritonitis Bro Follow-up: 6 months	118 per 1000	59 per 1000 (6 to 591)	RR 0.50 (0.05 to 5.01)	34 (1 study)	⊕⊕⊖⊖ low[1,2,3,4]
RCT- Exit-Site Infection Bro Follow-up: 6 months	59 per 1000	59 per 1000 (4 to 868)	RR 1.00 (0.07 to 14.72)	34 (1 study)	⊕⊕⊖⊖ low[1,2,3,4]
RCT Tunnel Infection Bro Follow-up: 6 months	0 per 1000	Can not calculate, since 0 events in the control group	RR 3.00 (0.13 to 68.84)	34 (1 study)	⊕⊕⊖⊖ low[1,2,3,4]
Observational study- peritonitis Sanchez Follow-up: 3 years	Only episodes per group reported		RR 0.46 (0.34 to 0.63)	237 (1 study)	⊕⊖⊖⊖ very low[1,2]

[1] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>),

[2] Only one study. Unclear reproducibility

[3] High drop-outs. In APD 4 of original 17, in CAPD 5 of original 17

[4] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

APD=automated peritoneal dialysis; CAPD=continuous ambulatory peritoneal dialysis; RR=relative risk

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

Our analysis of the observational study (24) showed significantly fewer cases of peritonitis in the APD group. None of the comparisons of infections (peritonitis, exit site infection and tunnel infection) from the RCT (14) showed any significant differences. We assessed the documentation for the outcomes peritonitis, exit-site infection and tunnel infection from the RCT to be of low quality. However, this RCT (14) was a very small study with only 34 patients, hence it is very likely that further research could give different results. The documentation for peritonitis from the observational study we assessed to be of very low quality, hence we have very little confidence in this effect estimate.

Quality of life

Bro *et al.* 1999 (14) reported quality of life measured by SF-36, but only in a figure. According to the article there was no difference in the changes of scores from start to end of study between patients treated with APD and CAPD.

The quality of the evidence for quality of life

We assessed the documentation for quality of life from the RCT to be very low. The reasons for downgrading the quality are shown in the footnotes to table 21.

Summary of findings for quality of life for APD home versus CAPD home

Table 21 below gives a summary of the comparative risks, the relative effects and the quality of the documentation for quality of life.

Table 21: *Summary of Findings Table for quality of life for APD home versus CAPD satellite*

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk CAPD	Corresponding risk APD			
RCT QoL Follow-up: 6 months	Only data from a figure			34 (1 study)	⊕⊖⊖⊖ very low[1,2,3]

[1] Only one study. Unclear reproducibility

[2] High drop-outs. In APD 4 of original 17, in CAPD 5 of original 17

[3] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

APD=automated peritoneal dialysis; CAPD=continuous ambulatory peritoneal dialysis.

For more details see the GRADE evidence profile (Appendix 6).

What do the results mean?

The documentation of quality of life came from one RCT (14), and we assessed this documentation to be of very low quality, hence we have very little confidence in this effect estimate.

Overall summary of the clinical results

Mortality

- We found no significant difference in mortality for the comparison PD home versus HD hospital and the comparison HD home versus HD satelitte. The quality of the documentation was low.
- Other comparisons (HD satellite versus PD home and APD versus CAPD) had very low documentation quality for mortality.

Complications

- We found significantly fewer hospitalisation days per patients per year for the patients in the HD hospital group than in the PD home group. The quality of the documentation was low.
- We found no significant difference in different types of infections (peritonitis, exit site infection and tunnel infection for the patients in the APD versus CAPD groups. The quality of the documentation was low.
- All other comparisons (HD satellite vs HD hospital, HD home versus HD satellite, HD satellite versus PD home, HD home versus PD home) had very low documentation quality for complications.

Quality of life

- We found no significant difference in quality of life for the the patients in the PD home and the HD hospital groups. The quality of the documentation was low.
- All other comparisons (HD satellite vs HD hospital, HD home versus PD home, APD versus CAPD) had very low documentation quality for this outcome.

Economic evaluation-Methods

General

We performed a cost-utility analysis (CUA) where relevant costs were expressed in 2012 Norwegian kroner (NOK), and effects were expressed in quality-adjusted life-years (QALYs). The analysis was carried out from both a societal and healthcare perspective (more detail about the costs included in the model from different perspectives is discussed later in this report; see page 74). Both costs and effects were discounted using an annual discount rate of 4% in accordance with Norwegian economic guidelines (9;30).

The results were expressed as mean incremental cost-effectiveness ratio (ICER) and mean incremental net health benefit from 1000 runs of the model in base-case. In the absence of an explicit threshold value for cost-effective interventions in Norway, we assumed the value (NOK 588,000 per QALY gained) recommended by the Norwegian Directory of Health as a best possible temporary estimate (9).

Uncertainties in model parameters were handled by performing one-way (tornado diagram) and probabilistic sensitivity analyses, designed as a Monte Carlo simulation, with 1000 iterations.

Model structure

In order to assess the cost-effectiveness of different dialysis modalities, a decision analytic model was developed in TreeAge pro ® 2012. The model is of the Markov type, in which a cohort of patients is followed over a given period of time. A Markov model was considered appropriate as end stage renal failure (ESRF) is a chronic condition requiring continuous treatment.

The model assumes that patients with severe renal failure begin in one of the dialysis modalities: hospital hemodialysis (HD hospital), self-care hemodialysis carried out in hospital (HD selfcare), satellite hemodialysis (HD satellite), home hemodialysis (HD home) and peritoneal dialysis (PD). Three states, HD home, HD satellite, and PD, include a stabilization and training period in the hospital. Transplantation is included in the model to present all of the possible modalities affording renal re-

placement therapy for ESRF patients, but only as absorbing state. Once an individual makes a transition into the absorbing state, no further incurred costs are included in the analysis.

Based on the Norwegian renal registry annual reports, median time from start of renal replacement therapy until death is 33-42 months (31). A 5-year time horizon was therefore used to assess the clinical and economic outcomes associated with each treatment strategy. The cycle length of the model was one year, meaning that any transitions between different states could happen only once per year. Patients could be in only one of the pre-defined states at any time. Upon completion of each cycle patients could, depending on transition probabilities, transfer to another state or remain in the same state until death or the end of the simulation. In addition, patients could experience complication events during each health state. Each state and event is associated with specific outcomes and costs.

A graphical representation of the model is shown in Figure 11 and Appendix 8.

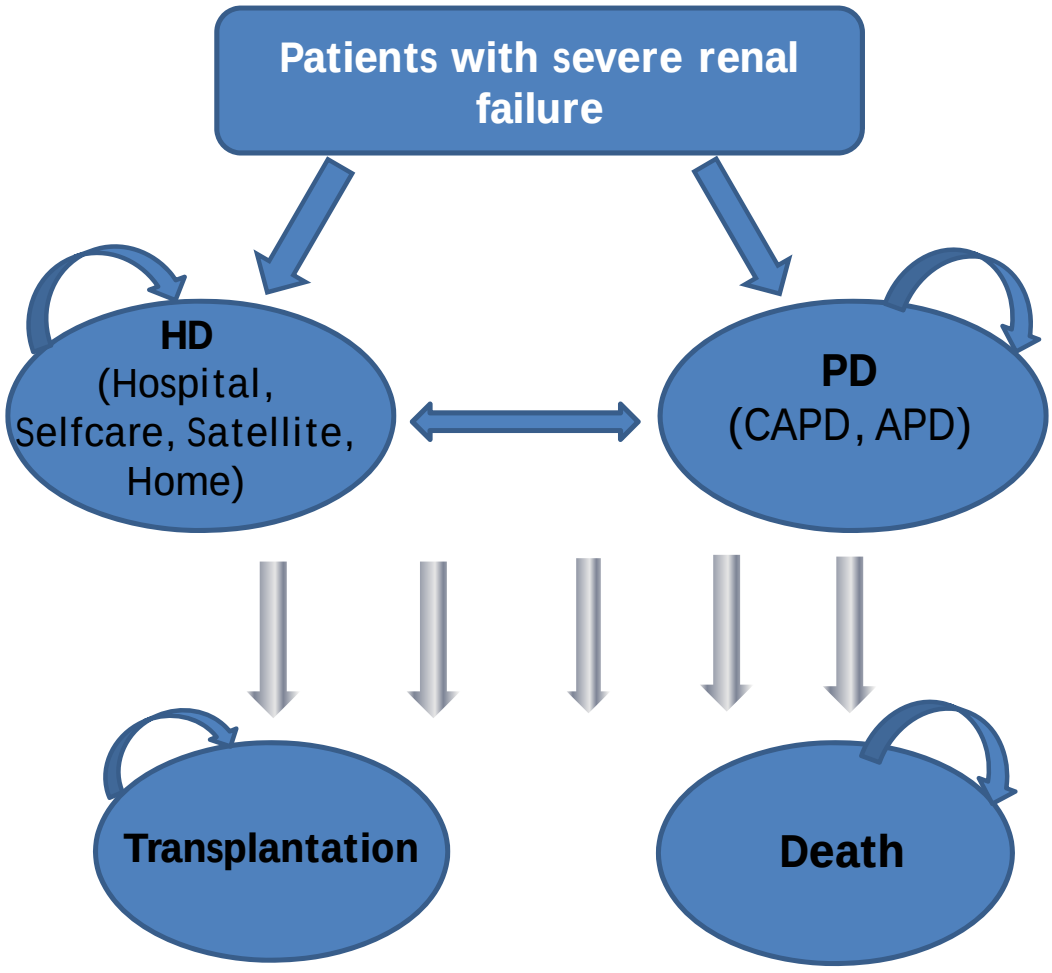


Figure 11. *Model structure (transplantation and death were included in the model only as "absorbing" states)* HD: hemodialysis; PD: peritoneal dialysis; CAPD: continuous ambulatory peritoneal dialysis; APD: automated peritoneal dialysis

Model Parameters

The sources and methods used to derive model parameters are described below:

Probabilities

The probability of transferring to another state or remaining in the same state was estimated based on Norwegian epidemiological data and clinical efficacy estimates.

The transition probabilities, *i*.e. the probability of starting on one modality and switching to another, are presented in Table 22. All of the base-line probabilities were based on data from the Norwegian renal registry (Personal communication by dr. med. Torbjørn Leivestad (32)) over a 5-year time horizon, *i.e*. a cohort of patients who started dialysis in 2007 and were followed for 5 years. The registry data was divided into HD, PD and transplant patients. The mortality probability for dialysis patients was not separated based on different dialysis modalities. The probability of mortality from each modality was therefore calculated by multiplying the annual probabilities of death for Norwegian dialysis patients by the estimate of relative risks of death from our systematic review. As previously noted, transplantation was assumed to be an absorbing state in the model. All probabilities were incorporated into the model as beta distributions.

Table 22. *Annual transfer probabilities based on Norwegian renal registry (32)*

	2007	2008	2009	2010	2011	2012
PD to HD	0.05	0.14	0.09	0.11	0.10	0
HD to PD	0.03	0.02	0.02	0.01	0	0
Dialyse-Transplant	0.07	0.13	0.12	0.09	0.08	0.07
Dialyse-death	0.10	0.14	0.19	0.23	0.21	0.25

HD: hemodialysis; PD: peritoneal dialysis

Clinical efficacy parameters in the model

Clinical efficacy data for the model was derived from our systematic review of the literature as presented earlier in this report (Figure 5 and Figure 9). The relative risks were added to the model as probability distributions. We used log-normal distributions, according to the methodology described by Briggs and co-authors (33). Standard errors for the log-normal distributions were calculated based on confidence intervals for efficacy estimates. The estimates related to the calculation of distributions for efficacy parameters used in the model are presented in Table 23.

Table 23. *Efficacy estimates for log-normal distribution*

	PD vs. HD hospital			**HD home vs. HD satellite**		
	RR	ln(RR)	SE	RR	ln(RR)	SE
All cause mortality	1.11 [a]	0.10	0.33	0.60	-0.51	0.31

HD: hemodialysis; PD: peritoneal dialysis; RR: relative risks; SE: standard error

[a] We used mortality data from the observational studies as the meta-analysis was based on several studies (Figure 5).

In addition, we found an observational study that reported the rate of PD mortality compared with HD satellite, for which we assessed the quality of documentation as very low (see Table 10). However, to evaluate the relative effectiveness of different dialysis modalities, we should use a common comparator in the model. Therefore, we assumed that there is no difference in mortality between the HD hospital and HD satellite and the estimate of relative risks of death presented in Table 23 was used in the model.

Costs

An annual cost per patient associated with the treatment modalities was calculated for each health state in the model. Our primary analysis was carried out from a healthcare perspective, *i.e.* only direct costs were calculated. In addition, we presented the results from a societal perspective, including direct health care costs as well as indirect costs related to dialysis treatment. We have attempted to identify and appreciate the differences between the treatment options and less emphasis on common elements.

Direct costs

Direct costs for dialysis care include costs associated with personnel (physicians, nurses and other involved personnel), medicines, supplies, laboratory tests, complications of the dialysis, training, as well as other costs borne by hospitals (*e.g.* costs associated with telemedicine communication for satellite units, capital and infrastructure costs) and transport cost.

All costs were measured in 2012 Norwegian kroner (NOK). Gamma distributions were applied for all cost parameters, with variation limited to 30% of the base-case value.

Personnel costs

The costs of personnel involved in dialysis treatment were calculated based on estimates of staff time per dialysis session for different treatment modalities. For peritoneal dialysis and HD home, the calculation was based on the time required for ini-

tiation of treatment, training of patient for the procedure, consultation and outpatient visits. The mean cost per hour was estimated based on the average healthcare staff salary per month from Statistics Norway (34) multiplied by 1.4 to account for social expenses (35). The costs of personnel involved in dialysis treatment are presented in Table 24 and Appendix 9.

Table 24. *Personnel costs per patient per month*

	Physician			Nurse			Other personnel [c]		
	Resource use (hours/ month) [a]	Unit cost (NOK) [b]	Costs (NOK)	Resource use (hours/ month) [a]	Unit cost (NOK) [b]	Costs (NOK)	Resource use (hours/ month) [a]	Unit cost (NOK) [b]	Costs (NOK)
HD hospital	5	557	2,785	60	383	22,980	13	473	6,149
HD self-care	5	557	2,785	39 [d]	383	14,937	13	473	6,149
HD satellite	5	557	2,785	60	383	22,980	13	473	6,149
HD home	2	557	1,114	5	383	1,915	1	473	473
PD	2	557	1,114	10	383	3,830	1	473	473

HD: hemodialysis; PD: peritoneal dialysis

[a] Based on data reported by Nyhus et al. 2007 (36) and expert opinion

[b] See Appendix 9 for details

[c] Incl. Secretary, medical technician, nutritionist, psychiatrist, physiotherapist, surgeon, operation room nurse

[d] Incl. time required for training of patient for procedure

It is also likely that additional training is required for nurses in the satellite units. The costs associated with additional training for nurses in the satellite unit were estimated based on costs reported by Bjorvatn (37). The estimated cost in 2012 for additional training for nurses in the satellite unit was NOK 12,000 per patient per year.

Costs of dialysis supplies

Costs of dialysis supplies for HD hospital were obtained from a Norwegian study based on data from three major hospitals in Norway (36). The costs were updated to 2012 costs. We assumed that the cost of consumable supplies for satellite and HD self-care was the same as the related costs for HD hospital. Costs of dialysis supplies for HD home were based on the price list provided by Oslo University Hospital (personal communication by head of dialysis department dr. med Aud-E Stenehjem). We estimated the consumable supplies costs for PD based on data from two suppli-

ers of PD consumables in Norway (Baxter and Gambro/Vingmed). The consumable costs for APD are more expensive than for CAPD. We estimated the costs for PD based on the assumption that 60% of PD patients use CAPD (32). The costs of dialysis supplies included in our model are presented in Table 25.

Table 25: *Costs of dialysis supplies per patient per week**

	Estimated costs (NOK)
CAPD	4,161 [a] (3,951-4,375)
APD	7,013 [a] (6,335-8,142)
Training PD	5,600 [b]
HD (hospital, self-care and satellite HD)	1,650 [c]
Training HD self-care	825 [d]
HD home	7,852 [e]
Training HD home	10,140 [e]

* Including VAT (value added tax)

CAPD: continuous ambulatory peritoneal dialysis; APD: automated peritoneal dialysis; PD: peritoneal dialysis; HD: hemodialysis

[a] Ref. Based on data from two suppliers of PD consumables in Norway (Baxter and Gambro/Vingmed)

[b] We assumed that PD patients need one week training at hospital; costs calculated based on average of CAPD and APD: NOK 5,600 per patient

[c] Ref. Based on data from three major hospitals in Norway (36); NOK 550 per dialysis session in 2012

[d] We assumed that HD self-care patients need one week training (3 dialysis sessions). The costs for initial dialysis treatments were assumed NOK 825 per patient.

[e] Ref. Based on the price list provided by Oslo University Hospital related to using NxStage home hemodialysis machine (personal communication by head of dialysis department dr. med Aud-E Stenehjem). HD home patients use different consumable supplies during the training period at the hospital (6 weeks) which the mean costs per week were estimated to be 10,140 per patient.

Medication costs

Drug costs were calculated based on maximum pharmacy retail prices (AUP) from Norwegian Medicines Agency (38). Drug doses were estimated based on treatment guidelines and expert opinion. In our analysis, we have only included costs associat-

ed with those medications for which considerable differences in use were reported for HD versus PD patients (based on data obtained from the Norwegian renal registry). The probabilities of drug consumption were incorporated as beta distributions in the model.

In addition, we included the cost associated with anticoagulation during hemodialysis (HD) therapy, and treatment of iron deficiency anemia (as different drugs and administration methods used for treatment of HD and PD patients) in our analysis.

We assumed identical drug costs for all HD modalities. Medication costs are presented in Table 26.

Table 26: *Costs of drugs per patient*

Drug group	Drug	Dosage [a]	Percentage of patients receiving the drug [b]		Price [c] (NOK)	Pills/ ampoules per package	Price per patient per year (NOK)		Price per patient per year without VAT (NOK)	
			HD	PD			HD	PD	HD	PD
Alpha-blocker	Doxazosin (Carduran)	1x8mg tablet per day	9%	12%	506.90	100	170	220	130	180
Calcium channel blocker	Amlodipine Besylate (Norvasc)	1x10 mg tablet per day	44%	53%	166.10	100	270	320	210	260
Diuretic	Furosemide (Diural)	4x250mg tablets per day	60%	78%	333.60	100	3,000	4,000	2,340	3,050
Erythropoiesis- stimulating agent	Epoetin alfa (Eprex)	HD: 100-180 units per kg per week [d] PD: 75 units per kg/week [d]	91%	83%	4549,3	6x1.0 ml [e]	33,120[f]	15,070[f]	26,500	12,050
Phosphate binder without calcium acetate	Sevelamer carbonate (Renvela)	2x800mg tablets per day	46%	51%	1707.10	180	3,190	3,540	2,550	2,830

Phosphate binder (with and without calcium acetate)	Calcium acetate and magnesium carbonate (Osvaren) Sevelamer carbonate (Renvela)	2x435mg/ 235mg tablets per day 2x800mg tablets per day	22%	12%	549.00 1707.10	180 180	2,010	1,110	1,610	890
Statin	Atorvastatin (Lipitor)	1x40mg tablet per day	55%	66%	279.20	100	560	670	450	540
Vitamin-D	Calcitriol (vitamin d3) (Rocaltrol)	1x0,25µg capsule per day	72%	79%	307.80	100	810	880	650	710
Anticoagulant treatment - HD	Daltaparin (Fragmin)	5000 units per dialysis	assumed for all HD Patients	-	3012,10	100x0.2 ml [g]	4,700	-	3,760	-
Iron	Iron sucrose (Venofer) Iron (Ferrous sulfate) (Duraferon)	HD: 1x100mg ampoule for 10 consecutive dialyses thereafter 1x100mg per week PD:1-2x100mg tablet(s) per day	assumed all dialysis patients were treated for iron deficiency anemia		755,00 119,90 [i]	5x5.0 ml [h] 100	23,600 -	- 660	18,900 -	- 530

VAT: value added tax; HD: hemodialysis; PD: peritoneal dialysis

[a] Based on expert opinion and treatment guidelines

[b] Based on data reported by the Norwegian renal registry

[c] Ref: Norwegian Medicines Agency (38)

[d] Ref: Muirhead 2005 (39)

[e] 1.0 ml contains 10,000 IU (84.0 micrograms) epoetin alfa

[f] The costs were estimated for a patient weighing 60 kg

[g] 0.2 ml=500 units

[h] 5.0 ml contains 20mg

[i] Fe^{3+}It is a non-prescription drug. Price was taken from http://www.apotek1.no

For HD patients, we also included parenteral nutrition costs based on the estimation reported by Nyhus and co-authors (36), which were updated to 2012 costs (approximately NOK 1,100 per dialysis session). We assumed 5-20% of HD hospital patients required parenteral nutrition (based on expert opinion, HD self-care and HD home patients needed less parenteral nutrition (5%-10%)).

Laboratory test costs

Annual laboratory test costs were calculated separately for HD and PD patients based on the standard blood tests for dialysis patients and the price lists provided by Oslo University Hospital (personal communication by head of dialysis department, dr. med Aud-E Stenehjem). Standard packages for blood tests for dialysis patients and yearly laboratory test costs are presented in Appendix 9 and Table 27.

Table 27. *Laboratory tests costs per patient per year (NOK)**

	HD	PD
Monthly test	589	580
Monthly test after dialysis	132	-
Additional test every 3 months	666	635
Additional test every 6 months	3,406	3,177
Total per patient / year	18,124	15,855

*Ref. Oslo university hospital (personal communication by head of dialysis department dr. med Aud-E Stenehjem)

HD: hemodialysis; PD: peritoneal dialysis

Complications costs

Based on our expert group's opinion, we have included two types of complications that require special measures in our model: infections and cardiovascular event. We included peritonitis, as the most common complication, and sepsis for peritoneal dialysis, while for hemodialysis infections (access-related infections and sepsis) and cardiovascular events were included in the analysis. Probabilities of the occurrence of these events were estimated based on data from the Norwegian renal registry (32). The registry reported the occurrence rate of the events at either end of the year (2011) or time of death, considering 220 patients on PD and 998 on HD (40). All rates were transformed into transition probabilities for use in the model.

Table 28: *Complications rate in Norway based on data from the Norwegian renal registry (32)*

Complications	Occurrence rate
Peritonitis-PD	0.44
Sepsis-PD	0.05
Sepsis-HD	0.11
Access related infections-HD	0.07
Cardiovascular events (percutaneous coronary interventions (PCI)) [a]	0.05

PD: peritoneal dialysis; HD: hemodialysis

[a] Due to lack of adequate information, we have only included percutaneous coronary interventions as cardiovascular complications in the analysis.

Probability of access-related hospitalisation and cardiovascular events were adjusted according to different dialysis modalities by multiplying the probabilities taken from Norwegian renal registry by the relative risks of these events from our systematic review (Table 29 and 30).

Table 29: *Relative risk of access related hospitalisation*

	HD hospital *vs.* HD satellite			HD home *vs.* HD satellite		
	RR	ln(RR)	SE	RR	ln(RR)	SE
Access related hospitalisation	1.14[a]	0.13	0.16	1.08[b]	0.08	0.28

HD: hemodialysis; RR: relative risks; SE: standard error

[a] See Table 7: Access related hospitalisation (HD hospital vs HD satellite)

[b] See Figure 10:Vascular access hospitalisation

Table 30. *Relative risk of cardiac or vascular hospitalisation*

	HD satellite *vs.* HD hospital			PD *vs.* HD hospital			HD home *vs.* PD		
	RR	ln(RR)	SE	RR	ln(RR)	SE	RR	ln(RR)	SE
Cardiac or vascular hospitalisation	0.53[a]	-0.63	0.33	0.03[b]	-3.51	1.43	1.45[c]	0.37	0.56

HD: hemodialysis; PD: peritoneal dialysis; RR: relative risks; SE: standard error

[a] See Table 7: Cardiac or vascular hospitalisation

[b] See Table 4: All acute coronary syndrome

[c] See Table 16: Patients admitted diagnosed with cardiac disease (angina, myocardial infarction, atrial fibrillation

The costs of treating infections associated with dialysis treatment have been calculated based on the treatment recommended in the National guidelines for antibiotic use in hospitals (41). We assumed patients received inpatient care for an average of 7-10 days per infection (expert opinion). The cost of cardiovascular events were calculated based on a Norwegian study (42). For cardiovascular events, we included the costs of two most common interventions related to coronary artery surgery (acute myocardial infection (AMI) and angina) in our analysis (43;44). The costs of treating septicemia were also estimated based on a Norwegian study (Wisløff et al. 2006(45)).

Complications costs are presented in Table 31.

Table 31: *Cost related to treatment of complications*

	Cost (NOK)	Description	Reference
Cost per peritonitis	1,594 70,000	Cefalotin [a] +ceftazidim [b] 1g/day; 2-3 weeks Average length of stay in hospitals:7 days	Norwegian guidelines for antibiotic use in hospitals; Norwegian Medicines Agency (38) Average cost per inpatient day: NOK10,000 (for medical wards of Norwegian hospitals)
Cost per access related infections	1,420 70,000	Kloksacillin [c] 2gx4/day; 10days Average length of stay in hospitals:7 days	Expert opinion; Norwegian Medicines Agency (38) Average cost per inpatient day: NOK10,000 (personal communication by senior advi-sor Ann Lisbeth Sandvik Department of Economy and Analysis, The Norwegian Directorate of Health)
Cost per acute myocardial infarction	161,898		Wisløff *et al.* 2012 (42)
Cost of developing angina and have treatment	122,088		Wisløff *et al.* 2012 (42)
Sepsis	111,317 [d]		Wisløff *et al.* 2006 (45)

[a] AUP pris: NOK 389 (10x1g)

[b] AUP pris:NOK548.50 (10x1g)

[c] AUP pris:NOK355.10 (10x2g)

[d] The costs were updated to 2012 costs.

The reduction in quality of life associated with complications is addressed in the next section.

Capital costs

Costs related to equipment (investment commodities) were estimated based on data from three major hospitals in Norway (36). Costs associated with water system, computers, ECG machine, infusion pump, blood pressure measure, warming plate and the other equipment (*e.g*. TV, beds furniture, weights iv-rack, etc) were included in the analysis. An equivalent annual cost was calculated for equipment items over

relevant life-spans for the items, using a 4% discount rate. The lifetime for the water system and the other equipment were set at 10 and 5 years, respectively. Capital costs associated with home HD treatment were estimated for using the NxStage machine, which requires less installation and reconstruction than standard hemodialysis machines (see Table 32).

Table 32: *Capital costs per patient per year*

	Costs per patient per year (NOK)
HD (hospital, self-care, satellite HD) [a]	44,838
HD home [b]	5,000
PD [a]	6,208

HD: hemodialysis; PD: peritoneal dialysis

[a] Ref. Nyhus *et.al* 2007 (36). The costs were updated to 2012 costs.

[b] Capital costs associated with using NxStage home hemodialysis machine. Ref. Personal communication by head of dialysis department at Oslo university hospital; dr. med Aud-E Stenehjem

Infrastructure costs

Infrastructure costs, *i.e.* administration costs/overhead costs, were calculated based on the costs reported by Nyhus and co-authors (36) and the estimates from Innlandet Hospital Trust (personnel communication by Kjell Nordaune; accounting department). The infrastructure costs for HD and PD were estimated to be approximately NOK 6570 and NOK 550 per patient per month, respectively. Due to uncertainly around the estimations, we varied overhead costs in the probabilistic sensitivity analysis. We used a gamma distribution with a standard error of 780.66 for HD and 75.06 for PD.

For HD home, we assumed the same overhead cost as PD (15 visits to the hospital per year[1]). Further, HD home patients were treated at the hospital in the training period (about 6 weeks). Overhead costs for HD satellite were estimated based on data reported by Bjorvatn (37). The costs were updated to 2012 prices (approximately NOK 8,553 per patient per month with a standard error of 1,309).

[1] Some patients need more than one visit per month plus training period for PD patients

Telemedicine

We included in our analysis the cost related to installation of telemedicine equipment for satellite units based on the costs reported by Bjorvatn (37). We calculated the cost based on the assumption of a 5-year lifetime for the telemedicine equipment and a discount rate of 4% per year. These costs were updated to 2012 costs (approximately NOK 11,000 -13,000 per patient, annually). Line rental for broadband was assumed to be NOK 12,000- NOK 18,000 per patient, annually.

Transport costs

The average distance traveled to the unit (hospital or satellite unit) was calculated based on data obtained from dialysis centers across the country. The average travel cost per mile (10 km) was estimated to be NOK 330 (personnel communication with "*Pasientreiser Telemark & Vestfold*"). It was assumed that the average number of hospital visits/treatments per year is 156 for HD hospital and HD satellite patients, and 15 for PD and HD home patients (incl. visiting a nephrologist and initial training). Moreover, we have estimated travel cost associated with initial of treatment (PD, HD home and HD satellite) and treatment of complications. Table 33 summarizes the information related to travel costs.

Table 33: *Travel costs per patient per year*

	Average distance per trip (km)	No. of trips per year	Travel cost per year (NOK)	Travel cost per year- complications (NOK)	Travel cost per year- training (NOK)
HD hospital	45 (1-340)	156	227,310	Mean 3 times per year: 4,371	
HD satellite	33 (1-160)	156	165,690		
Costs of travelling to hospital for satellite patients	416 (180-1,948)			Mean 3 times per year: 40,560	5 weeks (3 times /week): 202 800
HD home	400 (320-480)[a]	12-15	156,000-195,00	Mean 2-3 times per year: approx. 33,000	6 weeks (4 times/week): 312 000
PD	228 (14-1,734)	15 (incl. training)	110,910	Mean 3 times per year: 22, 181	Included in "No. of trips per year"

HD: hemodialysis; PD: peritoneal dialysis

[a:] Based on data from University hospital of North Norway

For HD satellite, we have also included the costs associated with staff travel (for nurses and physicians). Assuming one physician visit per month, the costs estimated

were NOK 500. The costs related to physician travel (one visit per month) and nurses travel (attending internal training; 3 times per year) were assumed to be approximately NOK 7,200 and NOK 3,600 per year based on costs reported by Bjorvatn (37).

Home care

A Norwegian study has shown that about 30-40% of PD patients required home care assistance related to the treatment (*e.g.* fluid exchange) (46). We also assumed that 10% -20% of HD home patients might require home care help. The estimated cost of one nurse visit (assumed one hour) was NOK 700 (47;48).

Indirect costs

We conducted our analyses from a "limited" societal perspective in order to present an estimate of costs that may be borne by patients and their families (*i.e.* value of lost time due to travel). Costs linked to productivity loss were not included in our analysis, as elderly patients account for an increasing fraction of patients on renal replacement therapy (49). The reported average age of the patient undergoing dialysis in Norway during the last 5 years is approximately 62 years (31). Moreover, the result of a cohort study among Norwegian dialysis patient indicated that none of the patients was working; two-thirds of patients were retired and the remaining one-third was receiving a disability pension benefit (50). Therefore, only the value of leisure time for patients and value of lost time for any accompanying people were included in the analysis.

Value of leisure time lost to travel was estimated by multiplying lost leisure time (4-8 hours) by the annual number of treatments and the national average hourly wage rate (approximately NOK 245 per hour) (50). For patients undergoing dialysis in the hospital (both HD hospital and HD self-care) and satellite unit, we assumed one working-day (7.5 hours) as lost leisure time per treatment. For patients undergoing treatment at home (HD home and PD), the estimated average number of hospital visiting days per year was 15 and the leisure time loss was assumed to be one working-day at each visit.

In addition, based on the assumption that 10% -50% of patients were accompanied by another person when visiting the medical center (hospital or satellite unit), we calculated the value of leisure time for the companions as shown in Table 34. We also assumed that companions did not participate in the labor market, therefore only the value of leisure time for companions has been included in the analysis.

In our analysis from the societal perspective, we have deducted value-added tax and other transfer payments to the government from the included direct costs.

We summarize the cost information described above in Table 34.

Table 34: *Summary of costs per patient per year for the dialysis modalities considered in the base-case analysis (NOK)*

	HD hospital	HD self-care	HD satellite	HD home	PD
Direct costs					
Personnel					
Physician	33,420	33,420	33,420	13,368	13,368
Nurse	275,760	179,244	287,760 [a]	22,980	45,960
Other personnel	73,790	73,790	73,790	5,680	5,680
Dialysis supplies	85,800	85,800	85,800	408,320	273,570
Dialysis supplies-training [b]		825		10,140	5,600
Medication [c]	105,685	84,235	105,685	96,420	26,282
Laboratory test	18,124	18,124	18,124	18,124	15,855
Complications	24,330	23,590	20,840	18,885	30,570
Capital costs	44,840	44,840	44,840	5,000	6,210
Infrastructure costs	74,030	74,030	102,640	6,565 [d]	6,565
Telemedicine [e]	0	0	27,600	0	0
Home care	0	0	0	27,405	89,425
Transport costs	227,310 [f]	227,310 [f]	165,700 [f]	160,000 [f g]	110,000 [f g]
Staff travel	0	0	10,800	0	0
Indirect costs					
Value of leisure time; patient	287,330	287,330	287,330	27,630 [g h]	27,630 [g]
Value of leisure time; companion	114,930 [i]	57,470 [j]	114,930 [i]	5,530 [j]	11,050 [i]

HD: hemodialysis; PD: peritoneal dialysis
[a] Incl. additional training for nurses

[b] Initial cost
[c] Incl. parenteral nutrition costs for HD patients (5%-20%)
[d] HD home patients were treated at the hospital in the training period (about 6 weeks) which infrastructure costs were estimated to be NOK 8,540 (initial cost)
[e] Incl. costs associated with line rental for broadband and telemedicine equipment
[f] Travel cost associated with complications and initial of treatment were presented in Table 33
[g] We assumed that PD patients and HD home patients visit the hospital 12-15 times per year
[h] Value of loss time because of travel during training period (6 weeks) was calculated to be NOK44,200 (initial cost).
[i] We assumed that 30% -50% of patients were accompanied by another person when visiting the medical center.
[j] We assumed that 10% -30% of patients were accompanied by another person when visiting the medical center.

Health-related Quality of Life

The systematic search described in the clinical methods section returned no articles reporting quality of life outcomes measured with instruments considered appropriate for cost-utility analyses (preference-based, health-related quality of life instruments). Many of the studies reported SF-36 quality of life scores, but did not provide the necessary information to convert these measures into EQ-5D utility scores. We searched further in Embase and Medline for systematic reviews and meta-analyses that reported quality of life for dialysis patients based on EQ-5D, 15D, SF-6D, TTO or SG utilities and found two relevant meta-analyses (51;52). Neither analysis revealed significant differences in mean utility scores of HD and PD patients, regardless of the utility instrument used. There was also little indication that quality of life for hemodialysis patients varied significantly with regard to treatment setting (hospital, satellite, self-care in hospital or home).

For consistency, and acknowledging that different utility instruments will yield different results, we focused on values based on EQ-5D, the most commonly used instrument. We examined all studies underlying the meta-analyses that reported EQ-5D values as the quality of life outcome. The literature search results highlighted the lack of good quality utility-related quality of life data for different dialysis modalities.

Given the lack of good quality data on health-related quality of life, we relied on a Swedish matched-case study (53) that reported EQ-5D values. Because neither meta-analysis found significant quality of life differences based on dialysis type or treatment setting and to avoid bias in favour of one of the modalities, we applied the standard error-adjusted mean of the HD and PD EQ-5D utilities reported in a Swedish study as the single QALY weight of 0.64 (0.34-0.75) for all types of dialysis in the model. This estimate was compatible with the results reported by Liem and co-authors (51) of a meta-analysis of quality of life results measured using the EQ-5D instrument. We assumed that all patients were in the same underlying health state on entering the model.

Sennfält and co-authors also reported a QALY weight for kidney transplant patients (0.86; 0.81-0.92), and an estimated value for utility losses associated with episodes of infection (0.02 per year under the assumption of five, 2-week infection episodes annually), which are included in our model (53).

Because of the lack of quality of life data for dialysis patients experiencing complications associated with cardiovascular events, utility losses associated with these events were estimated using the best available data, a Norwegian study of stroke patients from 2011 (54). We assumed that the reduction in utility resulting from complication events would last 2 weeks (based on expert opinion and (53)).

Beta distributions were used for all utility values used in the model. The mean values and standard errors of the utility (QALY) weights used in our model are presented in the Table 35.

Table 35: *Quality of life data (base-case)*

	QALY weight	SE	Method of elicitation	Sources
Patients on dialysis	0,54	0,105	EQ-5D	Sennfält *et al.* 2002 (53)
Patients with kidney transplant	0.86	0.028	EQ-5D	Sennfält *et al.* 2002 (53)
Infection	-0.19	0.010	EQ-5D	Sennfält *et al.* 2001 (53)
AMI	-0.27	0.03	EQ-5D	Lunde & Wisløff 2012 (54)
Angina	-0.22	0.03	EQ-5D	Lunde & Wisløff 2012 (54)
Sepsis	-0.28	0.12	EQ-5D	Korosec *et al.* 2006 (55)

QALY: quality-adjusted life year; SE:standard error; AMI: Acute myocardial infarction

Although the literature review mostly showed no significant differences between dialysis modalities, studies have noted that quality of life tended to be higher for patients treated in satellite units or treated at home. We therefore performed scenario analyses to test the assumption of the potentially higher quality of life associated with treatment at home or in satellite unit. These estimates were based on EQ-5D values reported by de Witt (56). The scores for satellite and hospital HD were 0.81 (SE: 0.05) and 0.66 (SE: 0.04), respectively. The same study also reported a utility value of 0.81 (SE: 0.03) for PD. We assumed HD home would be assigned the same

QALY weight as HD satellite (57;58), and that HD self-care had the same utility as HD hospital.

Economic evaluation – Results

The prevalence of chronic renal failure and, thus, the need for dialysis is constantly growing. Given the limited capacity of existing dialysis units and the expected increase in demand for dialysis, it is essential to examine the feasibility of relying more heavily on outpatient treatment modalities, particularly because there appear to be few modality-related differences in treatment outcomes. In addition, the recent development of a portable home hemodialysis machine could allow patients to move freely and lead normal lives. Based on this background, the main objective of the economic evaluation was to compare the effectiveness and costs of HD home, the most effective strategy, with the other dialysis modalities from both a societal and healthcare perspective.

Incremental cost–effectiveness estimates

Health care perspective

The results of the cost-effectiveness analysis from a healthcare perspective are presented in Table 36. This table provides information on the incremental cost and incremental effectiveness of HD home compared with the other dialysis modalities. The gain in utility from HD home compared with the other modalities was not substantial and the difference in effectiveness is mostly caused by the increase in survival of HD home compared with the other modalities.

Over a five-year time horizon, HD home dominated both HD hospital and HD satellite, *i.e.* it was both more effective and less costly. HD home in comparison with HD self-care and PD was more costly and more effective, with incremental cost-effectiveness ratios of NOK 1,651,099 and NOK 4,344,526, respectively. The ICERs were clearly above the suggested threshold for cost-effectiveness of NOK 588,000.

Table 36: *Results of the base-case cost-effectiveness analyses from a healthcare perspective (discounted); HD home versus HD hospital, HD satellite, HD self-care and Peritoneal Dialysis*

	Total costs (NOK)	Effects (QALYs)	Incremental cost (NOK)	Incremental effect (QALYs)	ICER (NOK/QALY)	INHB
HD home	2,183,425	1.8745				
HD satellite	2,549,188	1.7353	365,763	-0.1393	Dominated	-0,76
HD self-care	1,951,610	1.7341	-231,815	-0.1404	1,651,099	0.25
HD hospital	2,209,828	1.7340	26,403	-0.1405	Dominated	-0.19
PD	1,428,693	1.7080	-754,731	-0.1737	4,344,526	1.11

QALY: quality-adjusted life year; ICER: incremental cost-effectiveness ratio; INHB: incremental net health benefit; HD: hemodialysis; PD: peritoneal dialysis

Societal perspective

Table 37 illustrates the results of the base-case analysis from a societal perspective.

From a societal perspective and during the considered time horizon, HD home dominated the other hemodialysis methods, *i.e.* HD hospital, HD satellite and HD self-care, (both less costly and more effective). HD home also was more effective and at the same time, more costly relative to PD. The incremental cost per effect for HD home compared with PD was estimated at NOK 2,657,211 which is again clearly above the suggested threshold value of NOK 588,000.

Table 37: *Results of the base-case cost-effectiveness analyses from a societal perspective (discounted); HD home compared with Hospital, Satellite, Self-care Hemodialysis and Peritoneal Dialysis*

	Total costs (NOK)	Effects (QALYs)	Incremental cost (NOK)	Incremental (QALYs)	ICER (NOK/QALY)	INHB
HD home	1,705,865	1.8613				
HD satellite	2,629,801	1.7181	923,936	-0.1443	Dominated	-1.71
HD self-care	1,951,610	1.7169	388,161	-0.1444	Dominated	-0.80
HD hospital	2,371,729	1.7169	665,864	-0.1432	Dominated	-1.28
PD	1,230613	1.6825	-475,252	-0.1789	2,657,211	0,63

QALY: quality-adjusted life year; ICER: incremental cost-effectiveness ratio; INHB: incremental net health benefit; HD: hemodialysis; PD: peritoneal dialysis

Sensitivity analyses

Healthcare perspective

We performed Monte Carlo simulations with 1 000 draws from the input distributions for both perspectives (healthcare and societal perspective). Results of the simulations are presented as scatterplots in the cost-effectiveness plane and as cost-effectiveness acceptability curves (Figure 12-15).

The incremental cost-effectiveness scatterplot and cost-effectiveness acceptability curve from a healthcare perspective are shown in Figure 12 and 13. In Figure 12, HD home is the origin, and the dotted line presents one possible threshold for cost-effectiveness (WTP), here set at NOK 588,000 per QALY gained. In Table 38, we have presented the percentages of simulations that are in each quadrant of the plot and also below and above the WTP-line. The simulated ICERs for HD hospital and HD satellite were mostly located in upper left quadrant; *i.e.* they are dominated by HD home (47% and 68%, respectively). At the same time, the simulated ICERs for HD self-care HD and PD were mostly located in lower left quadrant below the WTP-line (66% and 88%, respectively).

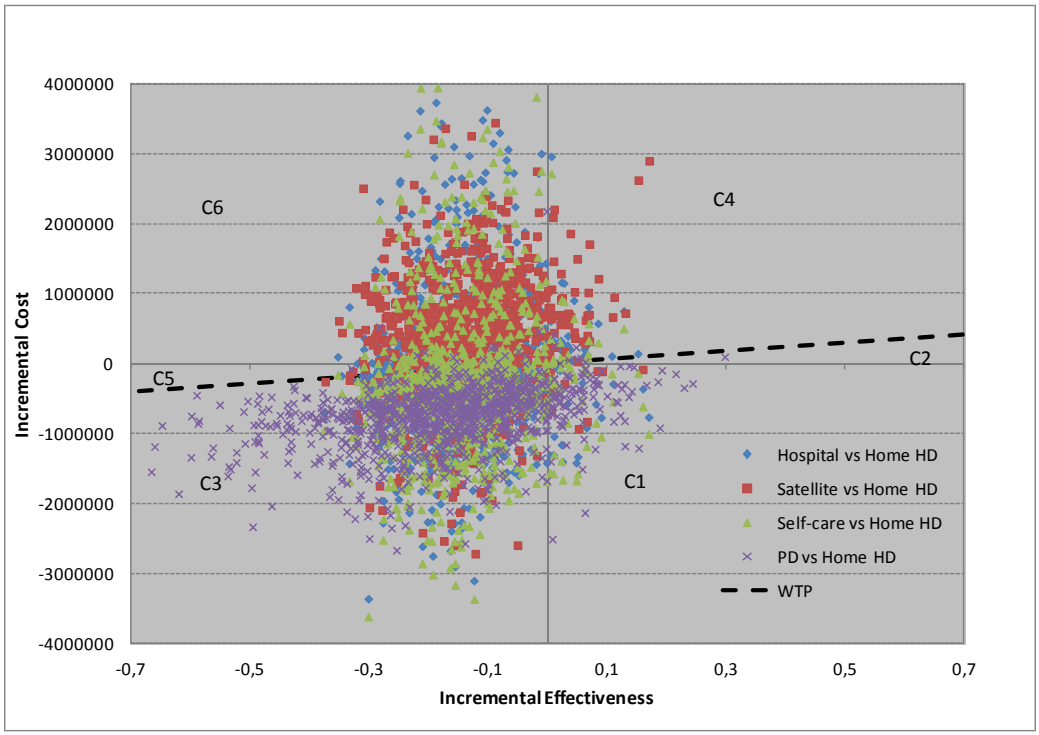


Figure 12. *Incremental cost-effectiveness scatter plot (healthcare perspective); HD: hemodialysis; PD: peritoneal dialysis*

Table 38: *Percentages of simulations in each quadrant of Figure 12*

Component	Incr. Eff.	Incr. Cost	ICER	HD hospital	HD satellite	HD self-care HD	PD
C1	IE>0	IC<0	Dominant	2%	1%	3%	9.5%
C2	IE>0	IC>0	<500 000	0%	0%	0%	0%
C3	IE<0	IC<0	>500 000	41%	22%	66%	88%
C4	IE>0	IC>0	<500 000	3%	5%	2%	1%
C5	IE<0	IC<0	>500 000	7%	4%	4%	1%
C6	IE<0	IC>0	Dominated	47%	68%	25%	1.5%

ICER: incremental cost-effectiveness ratio; HD: hemodialysis; PD: peritoneal dialysis

We also tried varying the willingness to pay from NOK 0 to NOK 1,000,000. The cost-effectiveness acceptability curves in Figure 11 show the probability of the alternatives being cost-effective subject to different levels of WTP. This figure indicates that PD was more likely to be the cost-effective strategy for all values of WTP. Assuming a WTP per QALY of NOK 588,000, the probability that PD was the most cost-effective strategy was 80%.

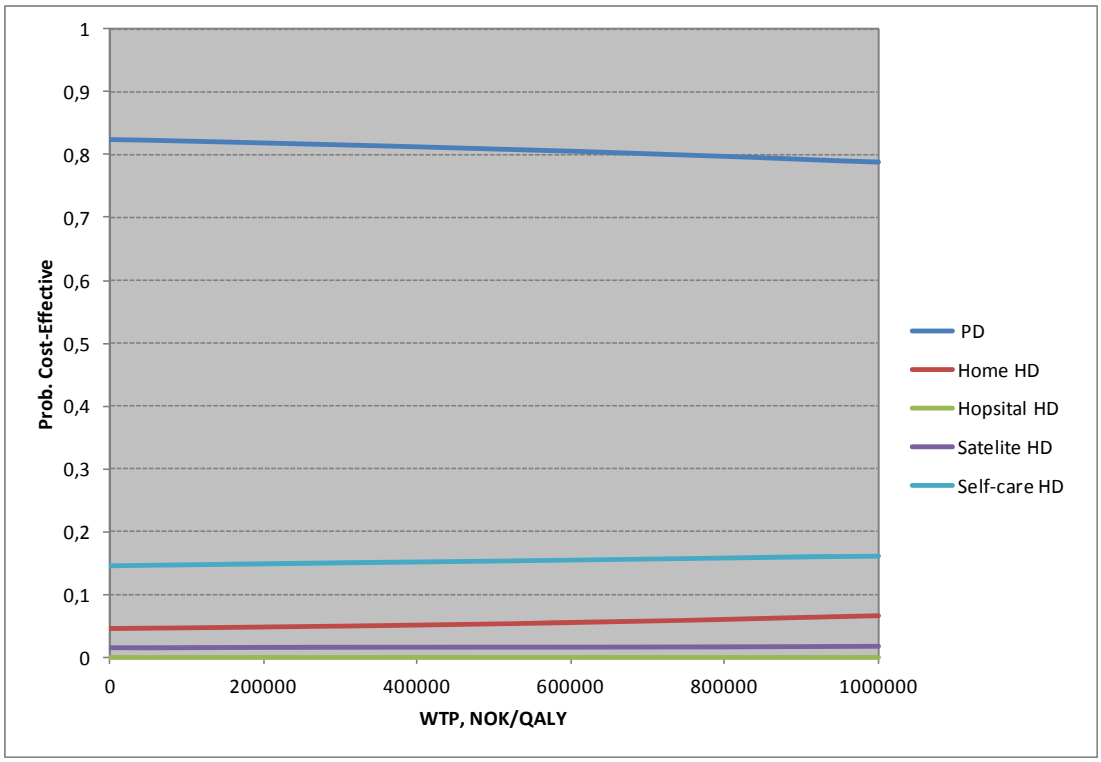


Figure 13. *Cost-effectiveness acceptability curves (healthcare perspective); PD: peritoneal dialysis; HD: hemodialysis; WTP: willingness to pay*

Societal perspective

Monte Carlo simulations with 1 000 draws from the input distributions are shown in Figure 14. In this figure, HD home is the origin, and the dotted line presents one possible threshold for cost-effectiveness (WTP), here set at NOK 588,000 per QALY gained. Figure 14 and Table 39 indicate that hemodialysis at hospital (conventional HD hospital and HD self-care) and satellite units were mostly dominated by HD home (82%, 70% and 89%, respectively). While the simulated ICERs for HD self-care and PD were mostly located in lower left quadrant below the WTP-line (66% and 88%, respectively).

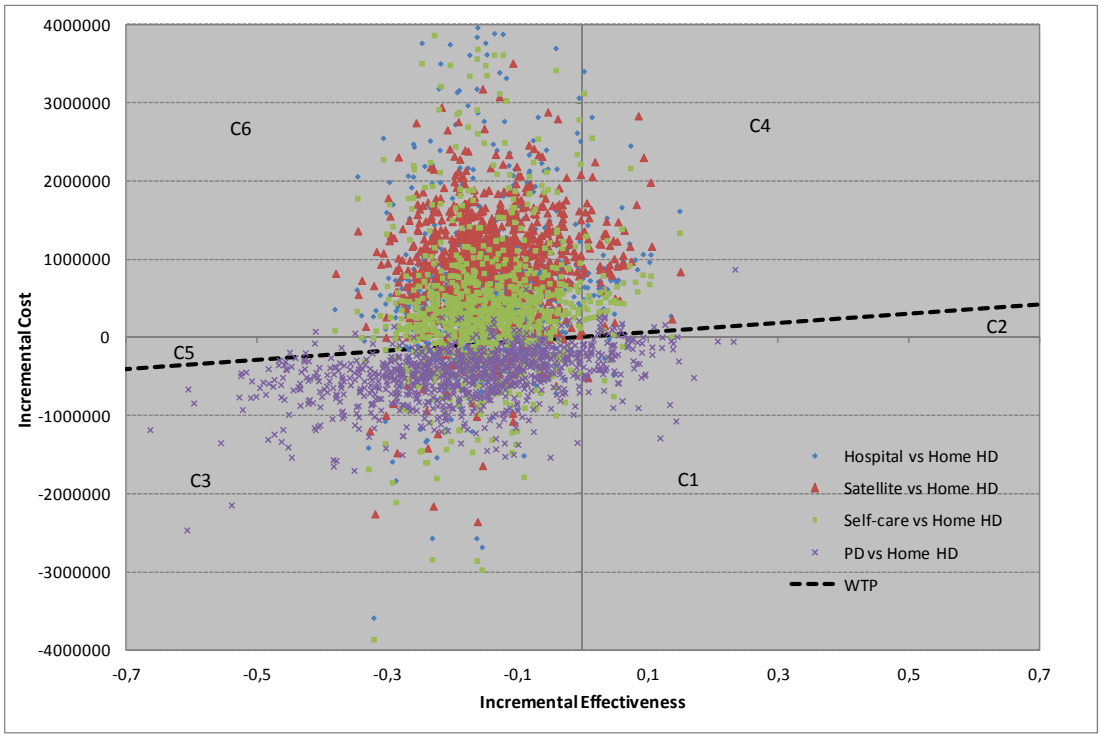


Figure 14. *Incremental cost-effectiveness scatter plot (societal perspective); HD: hemodialysis; PD: peritoneal dialysis*

Table 39: *Percentages of simulations in each quadrant of Figure 12*

Component	Incr. Eff.	Incr. Cost	ICER	HD hospital	HD satellite	HD self-care	PD
C1	IE>0	IC<0	Dominant	0%	0%	0%	8%
C2	IE>0	IC>0	<500 000	0%	0%	0%	1%
C3	IE<0	IC<0	>500 000	11%	5%	20%	84%
C4	IE>0	IC>0	<500 000	5%	5%	5%	2%
C5	IE<0	IC<0	>500 000	2%	1%	5%	3%
C6	IE<0	IC>0	Dominated	82%	89%	70%	3%

ICER: incremental cost-effectiveness ratio; HD: hemodialysis; PD: peritoneal dialysis

Figure 15 shows the probability of the alternatives being cost-effective subject to different levels of WTP from a societal perspective. This figure indicated that from a societal perspective, PD was also more likely to be the cost-effective strategy for all values of WTP. Assuming a WTP per QALY of NOK 588,000, the probability that PD was the most cost-effective strategy was 87%, while HD home had probability of 10% of being the most cost-effective strategy.

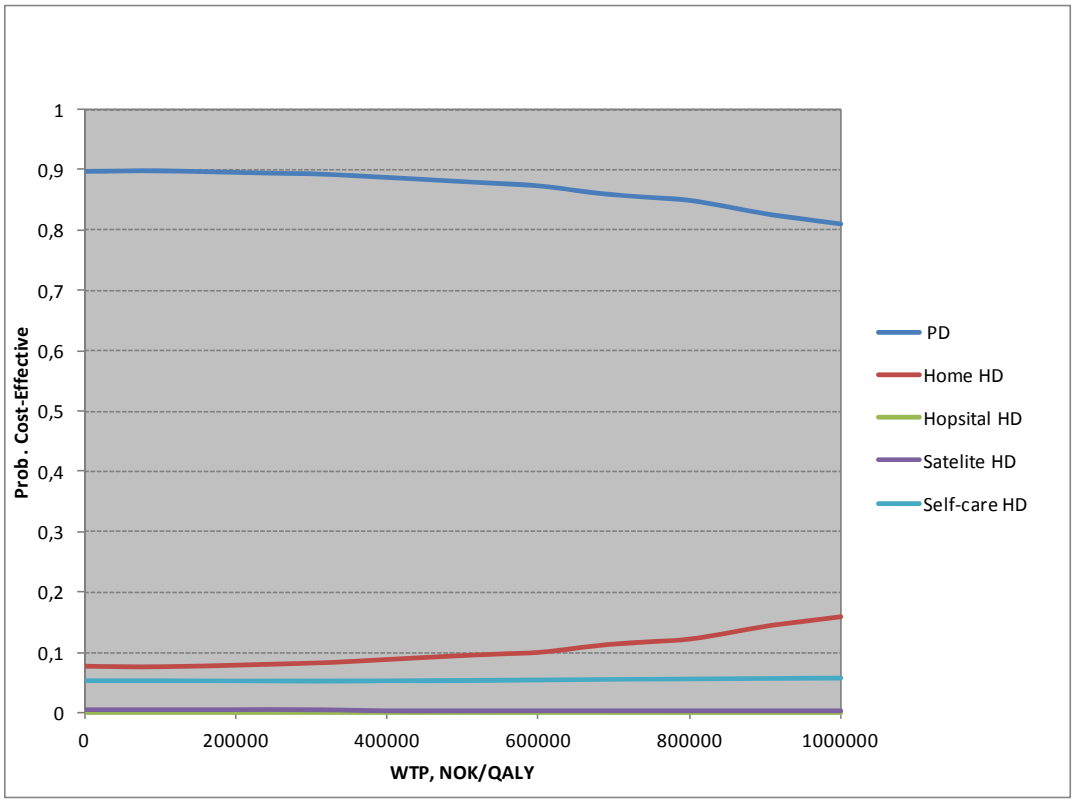


Figure 15. *Cost effectiveness acceptability curve (societal perspective); HD: hemodialysis; PD: peritoneal dialysis; WTP: willingness to pay*

Expected value of perfect information on parameters (EVPPI)

We also performed an analysis of the expected value of perfect information on all uncertain parameters to explore the uncertainty surrounding specific groups of parameters and show which group has the most impact on the results. EVPPI analyses were performed with 100x100 iterations. The EVPPI of different groups of parameters (costs, efficacy, QALYs and probabilities) are presented in Figure 16.

EVPPI was highest for cost data for all values of WTP, which indicates that the cost parameters have the greatest impact on decision uncertainty. These results suggest that if new research is to be undertaken, additional information on cost parameters would contribute most to reducing the uncertainty surrounding the decision about which treatment modality is most cost-effective.

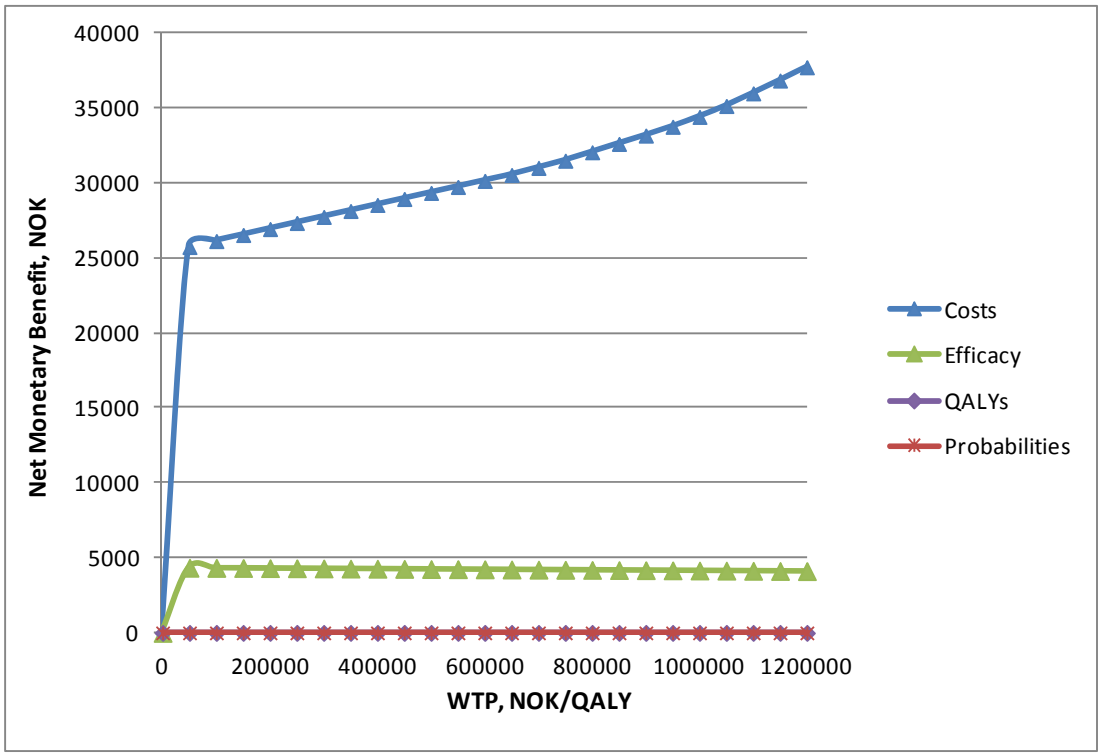


Figure 16. *Expected value of perfect information per patient for different groups of parameters; QALY: quality-adjusted life year; WTP: willingness to pay*

One-way sensitivity analysis (Tornado diagram)

A tornado diagram is a graphical method for displaying a series of one-way sensitivity analyses. Each parameter estimate was varied, individually, within reasonable bounds in order to investigate the impact on the results. We performed one-way sensitivity analyses separately for each comparison (HD home compared with the other dialysis modalities). Commonly the results were most sensitive to changes in distance per trip for different dialysis modalities, the mortality rates, cost of dialysis supplies, number of dialysis sessions per week, personnel cost (healthcare staff salary per month and standard number of working hours), travel cost per mile, overhead cost, and choice of discounted rate.

In the example shown in Figure 17, we present the top 10 variables that had a large potential impact on the results of HD hospital compared with HD home.

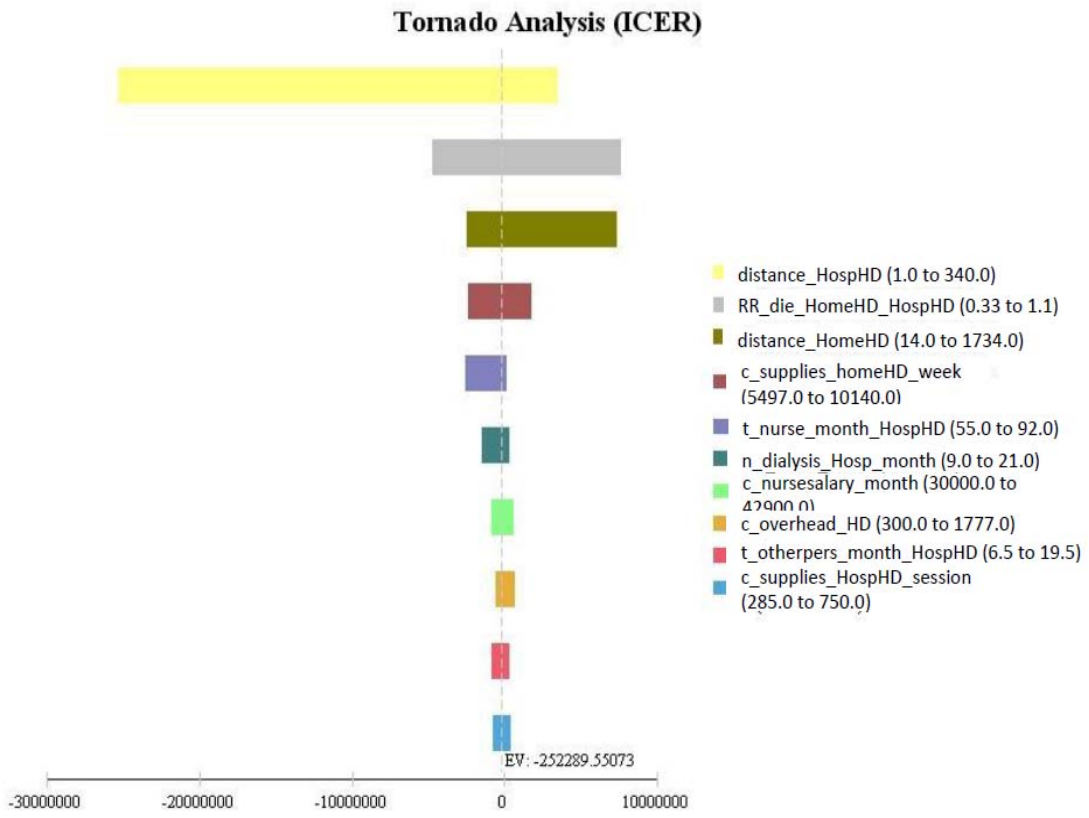


Figure 17. *The top 10 variables in tornado diagram of hemodialysis hospital compared with hemodialysis home*

Scenario analyses

As previously noted in this report, we could not identify good quality utility data and because neither meta-analysis found significant quality of life differences based on dialysis type or treatment setting, we applied a single QALY weight based on the best available data in base-case analyses. However, some studies observe that quality of life tended to be higher for patients treated in satellite units or treated at home. We performed scenario analyses to test the assumption of a potentially higher quality of life associated with treatment at home or in satellite unit. The correction factor had a very small effect on the results as treatment at home (PD and HD home) already was more cost-effective than the other dialysis modalities. However, HD satellite would experience increased costs and effectiveness relative to HD hospital from both a healthcare and societal perspective), with cost-effectiveness ratios of NOK 967,600 and NOK 725,700 per QALY gained, respectively, which is still above the suggested willingness to pay of NOK 588,000. The conclusion remained the same as in the original analysis.

Discussion

In this HTA we have systematically reviewed and summarized 18 studies examining adult patients receiving hemodialysis (HD) or peritoneal dialysis (PD) performed at different locations, specifically, hospital, home, satellite units or self-care in hospital. We focused on the impact on mortality, complications that require special measures (*i.e.* hospitalisation and antibiotic treatment) and quality of life.

We have further performed an economic evaluation to examine the relative cost-effectiveness in a Norwegian setting of different dialysis modalities (HD hospital, HD self-care carried out in hospital, HD satellite, HD home and peritoneal dialysis) from both healthcare and societal perspectives in patients with end stage renal disease.

Summary of results

Clinical

- We found no significant differences in mortality (PD home versus HD hospital, and for HD home versus HD satelitte); quality of life (PD home versus HD hospital) or in infections between the two types of peritoneal dialysis. The quality of the documentation was low.
- We found significantly fewer hospitalisation days per patients per year in the HD hospital group than in the PD group. The quality of the documentation was low.
- All other comparisons had very low documentation quality.
- Of 21 possible comparisons only six had published data.

The efficacy outcome used in the economic evaluation was mortality. Although the result showed no significant difference, there was a trend in favour of HD home.

Economic evaluation

- From a healthcare perspective: HD home was the dominant strategy relative to HD hospital and HD satellite (more effective and less costly). HD home

was more costly and more effective than HD self-care and PD although the incremental cost-effectiveness ratios (ICER; NOK 1,651,099 and NOK 4,344,526, respectively) were clearly above the suggested threshold for cost-effectiveness of NOK 588,000 per QALY gained.

- From a societal perspective: HD home dominated all other hemodialysis modalities (i.e. HD hospital, HD self-care and HD satellite). HD home was more costly and more effective relative to PD, but the ICER (NOK 2,657,211) was above the suggested threshold.
- The results of our sensitivity analysis showed that cost data had the greatest impact on the results' uncertainty.

Quality of documentation/model

The quality of the efficacy and safety documentation was assessed using GRADE. This tool helps us to systematically assess issues that may have an impact on our confidence in the accuracy of the estimates/results. As we only identified two small RCTs and used observational studies for our review, several issues lower our confidence in the estimates of effect. We assessed the documentations from the two RCTs to be of low quality. The documentation from the observational studies had low and very low quality. In the GRADE system outcome documentation from observational studies starts at low quality.

Our cost-effectiveness analysis showed that there is some uncertainty around the estimates. Most of the decision uncertainty arises as a result of uncertainty in the cost data, making it most reasonable to conduct further research on these parameters.

Strengths and weaknesses of this report

A strength of this HTA report is the use of a systematic literature search to identity all relevant articles. Further, data extraction, quality assessment and data-analyses were all done by one person and controlled by another to reduce the likelihood that important information was overlooked.

The strongest limitation is the low quality of the research documentation. Thus there is an uncertainty in the estimated effects, both whether observed differences are real or whether no differences is due to poorly designed studies.

Most of our documentation regarding effectiveness of the different dialysis modalities came from observational studies. Because observational studies are not based on

randomizing patients to different groups and hence, lack a random distribution of known and unknown factors among the groups, they are normally deemed to have a greater potential for differing patient characteristics across groups at baseline. We have however only assessed studies that either reported that groups did not differ significantly in comorbidity at baseline or provided enough baseline details for us to conduct tests for those differences. Differences in comorbidity at baseline could have influenced the results of comparisons of different dialysis modalities. The testing we have done to ensure no significant difference in comorbidity at baseline for the compared groups is therefore pivotal. Had this information been lacking, we would not have been able to distinguish differences reflecting different study group characteristics from differences reflecting the different interventions.

We limited our literature search to studies performed after 1995 because erythropoietin was introduced about that time. This shift in treatment may have had a clinical impact on the estimates of effect so focusing on this treatment regimen helps to ensure that the included studies are more comparable to current treatment.

Comparison of different *dialysis modalities*, as we have done, has both strengths and weaknesses. The strengths may be that such information is needed. The number of people with end stage renal disease has been increasing in recent years and is expected to increase in the future (5;59). Knowledge of the advantages and disadvantages of different types of dialysis and places of delivery may help to ensure better organization of care in the future and may aid in making better choices about the appropriate treatment for each patient.

Today most dialysis is hemodialysis in hospitals (40). There is an ongoing discussion, possibly reflecting the wishes of both patients and health authorities, about moving (or shifting) dialysis treatment from hospital/satellite to home (5;60). The thought is that this would be more convenient for the patient and less expensive for the community. The decision/recommendation to shift dialyses from hospital and/or from satellites to home should be based on documentation that ensures efficacy, safety and cost-effectiveness. A study like ours is designed to examine if this is the case. However, in the cases in which individual patients are not suited for one type of dialysis, it should be possible for patients and their physicians to choose a suitable dialysis modality based on each patient's clinical status, preferences and geographic limitations.

For this HTA we were asked specifically to focus on the type of dialysis and the delivery location. Consequently, we could not examine differences in dialysis frequency, dialysis adequacy, residual function or dialysis equipment, all of which could have influenced our results. However, the examined outcomes (mortality,

complications that require special measures and quality of life) were all important (final outcomes) for the patient.

When comparing efficacy and safety we normally prefer to use data from randomized controlled trials. However, we found only found 2 RCTs (14;19) out of our 4336 abstracts, which may be an indication that randomized controlled trials may not the be the most appropriate design for studying different types of dialysis. The reason for this could be both the strong wish from the patient for a specific treatment as well as the routines of the health professionals. The recruitment problems in Korevaar *et al.* 2003 (19) provide some support for this possibility. While we were unable to include many RCTs in our HTA, we have included 16 controlled observational studies with numbers of patients ranging from 28-11,238. Observational studies are recognized as a better mirror of real life effectiveness.

Another weakness in our HTA is the quality of the documentation. This was low for six outcomes, but for the majority of outcomes the quality was very low. A natural explanation for this is that most of the documentation came from observational studies that start at low quality when using GRADE, and as soon as we had one reason to downgrade in GRADE the quality fell to very low. According to GRADE we have limited confidence in the effect estimates of low quality. However, since it has been shown to be very difficult to perform randomized controlled trials for this type of patients, we believe that our results from observational studies with low quality are, in practice, the best possible we can obtain for this type of treatment.

Limitations of the health economic model

To the best of our knowledge, this is the first study that evaluates the relative costs and effects of all dialysis modalities from both the healthcare and societal perspective. It does, however, have a number of important limitations.

Any simulation model is a simplification of real life. Moreover, although we have tried to find the most robust and best evidence available, the data used in the model have limitations. Therefore limitations associated with the input data and the simplifications of our health economic model should be considered when interpreting the results.

Lack of data comparing different hemodialysis modalities (with regard to treatment setting) was the most important limitation of this study. This limitation was relevant to all parameters, *i.e.* effect, quality of life and costs.

Little research exists examining the costs of different dialysis modalities in Norway, making it difficult to obtain reliable cost information for the different modalities, particularly home and satellite, and with regard to geographical conditions and existing infrastructure in different regions. We discuss below specific ways in which the cost assumptions we used in the model may be less than ideal. Although we have tried to conduct our analysis based on best available data, and have incorporated uncertainty around cost estimates in the sensitivity analysis, the cost estimates need to be treated with some caution.

HD home and HD satellite units may require more skilled nurses than a hospital unit to compensate for the limited clinical staff. We did not include the costs of more skilled nurses or training of additional nurses in our analysis.

Lacking specific data, we assumed that the cost of consumable supplies was the same for HD hospital, HD satellite and HD self-care. It is possible, however, that the cost of supplies varies across settings.

The level of staffing for each modality may vary in different regions. Satellite care staffing, for example, could vary between that found in standard hospital units and that found in minimal care facilities. Thus, the variation in care level can have an impact on costs and cost-effectiveness estimates.

For HD home, we included the costs related to use of the new generation of home HD machine. Based on clinicians' opinions, these new machines can improve use and reduce both complication rates and the costs associated with installation and reconstruction.

Travel costs were difficult to assess because different portions are borne by patients, hospitals and public health care system. Unfortunately, none of the Norwegian Regional Health Authorities had a system that specifically registered travel costs related to dialysis treatment. Our analysis is therefore based on information obtained from dialysis centers across the country about the average distance travelled to hospital or satellite units.

Based on expert opinion, we included in our analysis only costs for treatment of major complications, that is, those requiring special measures and hospitalisation. This included costs related to treatment of peritonitis for peritoneal dialysis, and access related infections and percutaneous coronary interventions (AMI and angina) for hemodialysis. Costs related to more minor complications were not included.

We did not include the costs related to loss of production in our analysis as we assumed that most dialysis patients are of retirement age. However, we believe that including the cost of lost production may improve the cost-effectiveness for patients who are treated at home.

We performed a systematic literature search to identify the best possible evidence on utilities for our model. The search did not identify any single study or combination of studies reporting the utility values measured by a common instrument for all types of dialysis. Lacking good-quality utility data (preference-based health related quality of life data) for our study population, we applied a single QALY weight for all types of dialysis, based on a non-randomized Swedish study, which attempted to control for case-mix between PD and HD patients (53). However, because one could imagine that home or satellite dialysis patients might experience a higher quality of life than hospital hemodialysis patients, we performed scenario analysis to test of the implication of a potentially higher quality of life associated with these modalities. The correction factor, however, had a very small effect on the results and the conclusion in terms of cost-effectiveness was unchanged.

As mentioned earlier, effect estimates used in the model were mostly based on observational studies with low or very low quality of the evidence. Therefore, the efficacy estimates are associated with uncertainty.

In several cases, efficacy parameters used in the model are based on meta-analyses with no significant results. In this analysis we have used efficacy estimates whether or not the meta-analysis is statistically significant. In health economic evaluation it is a common practice to include no significant differences because, effect estimates themselves are considered to be the most likely outcome, and because it is assumed that the probability distributions represent the actual uncertainty.

Our results compared to other HTAs or economic evaluations

Efficacy and safety

We can compare our results with publications from 2003 from Great Britain (58) and from 2006 from Denmark (60).The following site comparisons are possible:

PD versus HD hospital

We found no significant difference in mortality between the groups. This we found both in one RCT (19) where we assessed the quality of the mortality documentation as low, and our meta-analysis of five observational studies (12;16;17;21;26) where we assessed the mortality documentation as very low. The Danish MTV has also studied

this comparison. They concluded that the RCT did not have sufficient power to conclude (38 patients). In our GRADE assessment we have also downgraded Limitation in Design by 1 to reflect this fact. The Danish MTV included several observational studies that show conflicting results. Four American studies (44;61-63) all showed that HD patients had longer survival than PD patients. Other (non-American) studies concluded the opposite, that PD patients had better survival than HD patients, at least for the first time after start of dialysis (64-67).

We used none of these studies in our assessment. The reasons for exclusions were either treatment period (before 1995) or that the localization for HD was not known. For more details see Appendix 2, Table III. It is noteworthy that none of the five observational studies (12;16;17;21;26) that we included were included in the Danish MTV. The reason for this is that three of those (12;16;21) were published after 2006, i.e. after their literature search; Vigneau *et al.* 2000 (26) is written in French (they only included studies in English and Scandinavian languages). It is unclear why they did not includ Jager *et al.* 2001 (17), an article reporting the Dutch NECOSAD I study. Our contact with the authors revealed that the hemodialysis was done in hospital.

Number of hospital days
We found significant fewer hospital days in the HD group than in the PD group. This is in agreement with findings reported in the Danish MTV (over a five year period the PD patients are hospitalized 10 days more than the HD patients). They based their results on a Danish register from 1990-2003 (68).

HD home versus HD satellite
We found no significant differences between the groups in mortality as well as hospitalisation due to vascular access and hospitalisation due to congestive heart failure. The quality of these outcomes was very low.

The HTA from 2003 from Great Britain (58) conducted similar comparisons to those in our HTA. They found that HD home was generally modestly better than HD satellite for survival and hospitalisation.

For mortality they used nine studies (69-77). All had treatment period before 1995 and were therefore excluded in our analysis. We have included Johansen *et al.* 2009 (18) and Weinhandl *et al.* 2012 (27), which were not included in the British HTA because they stopped their literature search in 2001. For hospitalisation they used two studies (78;79), which we considered but excluded. We excluded Mohr since that had cost as the main focus (they also looked at quality of life, but we excluded due to time before 1995 and because the location for HD was not known). We excluded

Bremer because of a treatment period before 1995. We have included Johansen *et al.* 2009 (18); this was not included in their HTA, since they stopped their literature search in 2001.

Health economics

We identified one HTA report that examined the cost effectiveness of dialysis in different treatment settings in the UK, but it was limited to comparisons of hospital, home and satellite treatment among hemodialysis patients (58). Economic modeling indicated that home hemodialysis dominated hospital hemodialysis, that is, it was less costly and more effective in terms of quality-adjusted life years. Relative to satellite treatment, home hemodialysis provided additional QALY benefits at a modest additional cost, £2215 and £3914, respectively at 5- and 10-year follow-up. However, we should mention that the costs of dialysis in different countries are difficult to compare because of different price systems and dialysis funding policies. Additionally, the defined patient groups (*e.g.* age, comorbidity, etc.) differed between studies.

We also found an HTA report from Denmark (60). Their review of the literature showed no significant differences in life expectancy between the various dialysis methods. Thus, their health economic evaluation was limited to cost considerations, where the expected development in numbers and distribution of dialysis patients were simulated over a 10-year period. The results showed that it would be cost-saving for the healthcare sector if the proportion receiving outpatient treatment rose from 30% to 40-45%.

Implications for practice

Our clinical results indicated no significant differences between the groups for mortality and quality of life (PD versus HD hospital) and for infections (APD versus CAPD, but significantly fewer hospitalisation days per patients per year in the HD hospital group than in the PD group. The quality of the documentation was low. It is therefore not possible to be certain which dialysis modalities should be preferred from an efficacy and safety point of view.

The result of our health economic analysis showed, however, that home dialysis modalities (PD and HD home) were the most cost-effective choices for dialysis patients, especially from the societal perspective. If home dialysis is not possible, it should be possible for patients and their physicians to choose a suitable dialysis modality based on each patient's clinical status and preferences.

Conclusion

All five dialysis modalities were almost equally effective in our analysis. When effects are combined with cost, hemodialysis at home was the most cost-effective alternative among the hemodialysis options. Peritoneal dialysis was the least expensive and hence the most cost-effective alternative compared to all hemodialysis modalities.

Need for further research

We acknowledge that performing randomized controlled studies in this population is difficult, but urge trialists to do their best to match study groups as well as possible and describe possible confounders.

There is considerable uncertainty around the cost estimates. Therefore, it is most reasonable to conduct further prospective studies on the costs associated with different dialysis modalities in Norway.

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Appendix

Appendix 1 – Literature search

Literature search - Dialysis modalities for patients with end- stage renal failure

Databases: The Cochrane Library: CDSR, DARE, Central, HTA, NHS EED.
Centre for Reviews and Dissemination: DARE, HTA, NHS EED.
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to present. EMBASE (Ovid) 1980 to present
Original search: 2012.05.10
Results: 109 Systematic reviews
4346 Controlled studies (Cochrane EPOC group –filter used in Ovid MEDLINE and Embase)
311 Health economic evaluations

Update search: 2013.08.08 (based on original search strategy)
Results: 38 Systematic reviews
879 Controlled studies (Cochrane EPOC group –filter used in Ovid MEDLINE and Embase)
70 Health economic evaluations
Searched by: Ingrid Harboe, research librarian

Search strategies

Syntax guide:

Symbol/ code:	Comment:
/ (slash)	Indicates MeSH/ Emtree terms in Ovid (e.g. hemodialysis/)
exp	explode, includes selected MeSH/ Emtree term and all narrow terms (e.g. exp hemodialysis/)
* (asterisk)	Used for truncation; searches for variations of a word (E.g. child* = child, children, childish…)
? (question mark)	Used for truncation; searches for one single character
adj6 (Ovid) near/6 (Cochr. L)	Requires words adjacent to each other with max. five words between them (in any order), use number 1-6 (adj1 = no word between the search words) Equal to adj6 in Cochrane library

use emez	Search (use) Embase
use prmz	Search (use) MEDLINE
.tw.	text word (word in title (.ti) or abstract (.ab))
kw	key word (in Cochrane Library)

Databases:
Federated search in:
Embase 1980 to 2012 Week 18 and
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present
Date: 2012.05.10

Search history:

1	hemodialysis/ use emez [emez = Embase]	57751
2	(haemodialy* or hemodialy*).tw.	117365
3	continuous ambulatory peritoneal dialysis/ use emez	11029
4	Peritoneal Dialysis, Continuous Ambulatory/ use prmz	9220
5	(peritoneal dialy* adj3 (ambulatory or automated)).tw.	13193
6	or/1-5 [Hemo or Peri]	154277
7	home dialysis/ use emez	1570
8	Hemodialysis, Home/ use prmz	1508
9	home.tw.	277128
10	Self Administration/	14683
11	(self adj2 (admin* or care)).tw.	73235
12	"hospital subdivisions and components"/ use emez [UF hospital units/ self care units]	10937
13	Hemodialysis Units, Hospital/ use prmz	1177
14	((hospital? or satellite) adj6 (unit? or subdivision? or department?)).tw.	125432
15	(centre* or center* or incentre or incenter).tw.	1002968
16	or/7-15 [lokasjon/admin.]	1443895
17	6 and 16 [Hemo/ Peri & Lokasjon]	15370
18	limit 17 to "reviews (maximizes specificity)"	79
19	systematic* review*.tw.	81177
20	17 and 19	43
21	18 or 20 [SR Emb. / Medl.]	82
22	remove duplicates from 21 [SR Emb. / Medl.]	56
23	randomized controlled trial/ [EPOC-filter Embase]	647854

24	Controlled Clinical Trial/	472367
25	Quasi Experimental Study/	1013
26	Pretest Posttest Control Group Design/	140
27	Time Series Analysis/	11562
28	Experimental Design/	73038
29	Multicenter Study/	240912
30	(randomis* or randomiz* or randomly or random allo-cat*).ti,ab.	1044957
31	groups.ab.	2549222
32	(trial or multicentre or multicenter or multi centre or multi center).ti.	275282
33	(intervention* or controlled or control group or compare or compared or (before adj5 after) or (pre adj5 post) or pretest or pre test or posttest or post test or quasiexperiment* or quasi experiment* or evaluat* or effect or impact or time series or time point? or repeated measur*).ti,ab.	12498679
34	or/23-33	13774574
35	(systematic review or literature review).ti.	74257
36	"cochrane database of systematic reviews".jn.	12227
37	Nonhuman/	3832807
38	or/35-37	3918222
39	34 not 38	12172742
40	17 and 39 use emez	5021
41	randomized controlled trial.pt. [EPOC-filter Medline]	326994
42	controlled clinical trial.pt.	84070
43	multicenter study.pt.	143233
44	(randomis* or randomiz* or randomly allocat* or random allocat*).ti,ab.	742187
45	groups.ab.	2549222
46	(trial or multicenter or multi center or multicentre or multi centre).ti.	275282
47	(intervention* or controlled or control group or compare or compared or (before adj5 after) or (pre adj5 post) or pretest or pre test or posttest or post test or quasiexperiment* or quasi experiment* or evaluat* or effect or impact or time series or time point? or repeated measur*).ti,ab.	12498679
48	or/41-47	13578567

49	exp Animals/	17744662
50	Humans/	25615589
51	49 not (49 and 50)	5037406
52	review.pt.	3527139
53	meta analysis.pt.	33493
54	news.pt.	150826
55	comment.pt.	503754
56	editorial.pt.	710888
57	cochrane database of systematic reviews.jn.	12227
58	comment on.cm.	503753
59	(systematic review or literature review).ti.	74257
60	or/51-59	9624455
61	48 not 60	10724278
62	17 and 61 use prmz	3443
63	40 or 62	8464
64	limit 63 to yr="1995 -Current"	7293
65	remove duplicates from 64	7293
66	65 use emez [Embase]	4398
67	65 use prmz [Medline]	2895
68	"Cost Benefit Analysis"/ [Filter: Cost effect./-utility]	113918
69	"Cost Effectiveness Analysis"/	79644
70	"Cost Minimization Analysis"/	2042
71	"Cost Utility Analysis"/	4079
72	(cost* adj2 (analys* or benefit* or effective* or minim* or utilit*)).tw.	187214
73	cba.tw.	17236
74	cea.tw.	33494
75	cua.tw.	1498
76	Economic Evaluation/	7042
77	Health economics/	30869
78	(health economic? or economic evaluation?).tw.	18445
79	Pharmacoeconomics/	6651
80	((pharmacoeconomic? or pharmac*) adj economic?).tw.	727

81	(15D or HRQoL or health-related quality of life instrument).tw.	15367
82	or/68-81 [Embase Filter: Cost effect./-utility]	395059
83	Cost-Benefit Analysis/	113918
84	(cost* adj2 (analys* or benefit* or effective* or minim* or utilit*)).tw.	187214
85	cba.tw.	17236
86	cea.tw.	33494
87	cua.tw.	1498
88	Economics, Medical/	39332
89	(health economic? or economic evaluation?).tw.	18445
90	Economics, Pharmaceutical/	6651
91	(pharmac* adj economic?).tw.	727
92	pharmacoeconomic?.tw.	7493
93	Technology Assessment, Biomedical/	18838
94	technology assessment?.tw.	6620
95	(15D or HRQoL or health-related quality of life instrument).tw.	15367
96	or/83-95 [Medline Filter: Cost eff./ -utility]	384560
97	17 and 82	699
98	97 use emez [Embase econ ev]	445
99	17 and 96 use prmz [Medline econ ev]	226

Database: Cochrane library

Date: 2012.05.10

#1	(haemodialy* or hemodialy*):ti,ab,kw	4553
#2	MeSH descriptor Peritoneal Dialysis, Continuous Ambulatory, this term only	431
#3	(peritoneal dialy* near/3 (ambulatory or automated)):ti,ab,kw	616
#4	(#1 OR #2 OR #3)	5052
#5	MeSH descriptor Hemodialysis Units, Hospital, this term only	22
#6	MeSH descriptor Hemodialysis, Home, this term only	47
#7	MeSH descriptor Self Administration, this term only	588

#8	(((hospital* or satellite) near/6 (unit* or subdivision* or department*)) or home):ti,ab,kw	17904
#9	(centre* or center* or in centre or incenter):ti,ab,kw	30288
#10	(#5 OR #6 OR #7 OR #8 OR #9)	46982
#11	(#4 AND #10)	451

Database: Centre for Reviews and Dissemination
Date: 2012.05.10

1	(haemodialy* or hemodialy*)
2	MeSH DESCRIPTOR Peritoneal Dialysis, Continuous Ambulatory
3	(Continuous Ambulatory Peritoneal Dialysis)
4	(Automated Peritoneal Dialysis)
5	#1 OR #2 OR #3 OR #4
6	MeSH DESCRIPTOR Hemodialysis Units, Hospital
7	MeSH DESCRIPTOR Hemodialysis, Home
8	MeSH DESCRIPTOR Self Administration
9	(hospital unit* or satellite unit* or hospital subdivision* or satellite subdivision* or hospital department* or satellite department*)
10	(home)
11	(centre* or center* or in centre or incenter)
12	#6 OR #7 OR #8 OR #9 OR #10 OR #11
13	#5 AND #12
14	(#13) IN NHSEED FROM 1995 TO 2012
15	#6 OR #7 OR #8 OR #9 OR #11
16	#5 AND #15
17	(#16) IN NHSEED FROM 1995 TO 2012
18	(#16) IN DARE, HTA FROM 1995 TO 2012

Ongoing studies

Source: WHO International Clinical Trials Registry Platform Search Portal

Date: 2013.08.09
Search: Title: kidney disease AND
Condition: hemodialysis or haemodialysis or peritoneal dialysis or kidney disease AND
Intervention: home or self administration or ambulatory or automated
Result: 69 trials

Source: Clinical Trials.gov

Date: 2013.08.09

Search: Conditions: kidney disease AND
Interventions: hemodialysis or haemodialysis or peritoneal dialysis

Result: 44 studies

Appendix 2- List of excluded studies

Table I: *Excluded SRs and HTAs*

Study References	Cause for exclusion of study
Home haemodialysis is an effective alternative to hospital or satellite unit haemodialysis. Evidence-Based Healthcare and Public Health 2005;9(2):123-4.	Abstract from Mowatt 2004
Bowman GS, Martin CR. Evidence of life quality in CAPD patients and implications for nursing care: a systematic review. Clinical Effectiveness in Nursing 1999;3:112-23.	No controll group
Cameron JI, Whiteside C, Katz J, Devins GM. Differences in quality of life across renal replacement therapies: A meta-analytic comparison. Am J Kidney Dis 2000;35(4):629-37.	Not our outcomes (emotional distress and phychological well-being
Canadian Agency for Drugs and Technologies in Health. Portable home hemodialysis for kidney failure.: Canadian Agency for Drugs and Technologies in Health (CADTH); 2007.	No controll group
Estrada MD. Peritoneal dialysis versus in-center hemodialysis: benefit, risk, cost and preferences.: Catalan Agency for Health Information, Assessment and Quality (CAHIAQ) - formerly CAHTA; 2010.	Spanish without english abstract
Ghahramani N, Shadrou S, Hollenbeak C. A systematic review of continuous renal replacement therapy and intermittent haemodialysis in management of patients with acute renal failure. Nephrology 2008;13:570-8.	Acute kidney failure
Glover C, Banks P, Carson A, Martin CR, Duffy T. Understanding and assessing the impact of end-stage renal disease on quality of life: A systematic review of the content validity of self-administered instruments used to assess health-related quality of life in end-stage renal disease. Patient 2011;4(1):19-30.	Not our outcomes (validity of QoL instruments)

Gonzalez-Perez JG, Vale L, Stearns SC, Wordsworth S. Hemodialysis for end-stage renal disease: A cost-effectiveness analysis of treatment options. Int J Technol Assess Health Care 2005;21(1):32-9.	No efficacy/safety data
Kellum JA, Angus DC, Johnson JP, Leblanc M, Griffin M, Ramakrishnan N, et al. Continuous versus intermittent renal replacement therapy: A meta-analysis. Intensive Care Med 2002;28(1):29-37.	Acute kidney failure
Kirby L, Vale L. Dialysis for end-stage renal disease: Determining a cost-effective approach. Int J Technol Assess Health Care 2001;17(2):181-9.	Report about an economical model (refers to McLeod)
MacLeod A, Grant A, Donaldson C, Khan I, Campbell M, Daly C, et al. Effectiveness and efficiency of methods of dialysis therapy for end-stage renal disease: a review. Health Technol Assess 1998;2(5):1-166.	This is a HTA/SR over RCT's. They compared differernt things that were not relevant for our PICO (1. Two types of membranes; 2. Two different buffers; 3. Different frequency; 4. Different delivery systems). Further: 5. *CCPD (APD) vs CAPD.* Here one study from 1994 (de Fijter et al). 6: *HD versus CAPD.* Here they did not find any RCTs
Mowatt G, Vale L, Perez J, Wyness L, Fraser C, MacLeod A, et al. Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of home versus hospital or satellite unit haemodialysis for people with end-stage renal failure.: Health Technology Assessment; 2003.	HTA/SR: Included 27 studies (4 SR, 1 randomized cross over and 22 comparative observational studies). Why we excluded: QoL: 16 studies: *3 SRs* from after 1997 (Cameron 2000: out due to outcome; Mohr 2001:Out no relevant data; Parson 1997: Out no actual studies) *13 comparative observational*: 11 of those out since from before 1995; Courts 1998: out due to outcome and Woods 1996: out due to time period, included from 1986-1987). Mortalitet: Here we have already included the actual studies. Hospitalization rates: Two studies (Mohr et al 2001:excluded focus is cost, also include QoL, but before 1995 and localization of HD unknown; Bremer et al 1989: Excluded due

	to treatment time)
Mowatt G, Vale L, MacLeod A. Systematic review of the effectiveness of home versus hospital or satellite unit hemodialysis for people with end-stage renal failure. Int J Technol Assess Health Care 2004;20(3):258-68.	This is an article of the HTA from 2003
Pannu N, Klarenbach S, Wiebe N, Manns B, Tonelli M. Renal replacement therapy in patients with acute renal failure: a systematic review. JAMA 2008;299(7):793-805.	Acute kidney failure
RJ, Varela LL, Sanchez IE, Ruano RA. Daily hemodialysis vs conventional hemodialysis: systematic review of clinical results and economic analysis.: Galician Agency for Health Technology Assessment (AVALIA-T); 2007.	Equivalent to Punal 2008
Punal RJ, Varela LL, Ruano RA. Clinical effectiveness of two frequencies of chronic hemodialysis: conventional versus short daily. Systematic review. 2007.	Equivalent to Punal 2008
Punal J, Lema LV, Sanhez-Guisande D, Ruano-Ravina A. Clinical effectiveness and quality of life of conventional haemodialysis versus short daily haemodialysis: a systematic review. Nephrology Dialysis Transplantation 2008;23(8):2634-46.	Sites not defined We do handsearch from the primary studies
Purins, A, Hiller JE. NxStage System One home Dialysis for patients waiting for kidney transplantation.: Adelaide Health Technology Assessment (AHTA) on behalf of National Horizon Scanning Unit (HealthPACT and MSAC); 2008.	Not our focus (device)
Rabindranath KS, Strippoli GF, Roderick P, Wallace SA, MacLeod AM, Daly C. Comparison of hemodialysis, hemofiltration, and acetate-free biofiltration for ESRD: systematic review. Am J Kidney Dis 2005;45(3):437-47.	Not relevant comparators
Roderick P, Nicholson T, Armitage A, Mehta R, Mullee M, Gerard K. An evaluation of the costs, effectiveness and quality of renal replacement therapy provision in renal satellite units in England and Wales.: Health Technology Assessment; 2005.	HTA, but not as a systematic review. In their Part 2 they have results from a primary controlled study (comparing HD satelitte with HD hospital). We have excluded this as a HTA/SR, but included as a controlled study (hand search)
Selgas R, Cirugeda A, Fernandez-Perpen A, Sanchez-	Not SR We do hand search from the primary studies

Tomero JA, Barril G, Alvarez V, et al. Comparisons of hemodialysis and CAPD in patients over 65 years of age: a meta-analysis. Int Urol Nephrol 2001;33(2):259-64.	
Suri RS, Nesrallah GE, Mainra R, Garg AX, Lindsay RM, Greene T, et al. Daily hemodialysis: a systematic review. Clinical journal of the American Society of Nephrology : CJASN 2006;1(1):33-42.	Unclear with respect to controll group and sites We do hand search from the primary studies
Tonelli M, Manns B, Feller-Kopman D. Acute renal failure in the intensive care unit: a systematic review of the impact of dialytic modality on mortality and renal recovery. Am J Kidney Dis 2002;40(5):875-85.	Acute kidney failure
Vale L, Cody JD, Wallace SA, Daly C, Campbell MK, Grant A, et al. Continuous ambulatory peritoneal dialysis. Cochrane Database of Systematic Reviews 2004.	Cochrane SR Only one RCT: Korevaar 2003, only as abstract. The title of the abstract is the same as the Korevaar 2003 we have included from our own search.

Table II: *Excluded controlled studies (randomized controlled trials) and observational studies*

Study References	Cause for exclusion of study
Home haemodialysis is an effective alternative to hospital or satellite unit haemodialysis. Evidence-Based Healthcare and Public Health 2005;9(2):123-4.	Abstract from Mowatt 2004
Adeniyi M, Kassam H, Agaba EI, Sun Y, Servilla KS, Raj DS, et al. Hospitalizations in patients treated sequentially by chronic hemodialysis and continuous peritoneal dialysis. Adv Perit Dial 2009;Conference on Peritoneal Dialysis. 25(pp 72-75):-75.	Not our outcome
Alloatti S, Manes M, Paternoster G, Gaiter AM, Molino A, Rosati C. Peritoneal dialysis compared with hemodialysis in the treatment of end-stage renal disease. Journal of nephrology 2000;13(5):331-42.	Overview, not SR. We have checked the included aricles.
Alwakeel JS, Alsuwaida A, Askar A, Memon N, Usama S, Alghonaim M, et al. Outcome and complications in peritoneal dialysis patients: a five-year single center experience. Saudi Journal of Kidney Diseases and Transplantation 2011;22(2):245-51.	The results were not specified for the different dialyses sites

Ansell D, Roderick P, Hodsman A, Ford D, Steenkamp R, Tomson C. UK renal registry 11th annual report (December 2008): Chapter 7 survival and causes of death of UK adult patients on renal replacement therapy in 2007: National and centre-specic analyses. Nephron - Clinical Practice 2009;111(SUPPL. 1):c113-c139.	Sites not specified
Baiardi F, Esposti ED, Cocchi R, Fabbri A, Sturani A, Valpiani G, et al. Effects of clinical and individual variables on quality of life in chronic renal failure patients. Journal of nephrology 2002;15(1):61-7.	Compare HD and PD, but HD included both hospital and satellite without separating the results.
Bhaskaran S, Schaubel DE, Jassal SV, Thodis E, Singhal MK, Bargman JM, et al. The effect of small solute clearances on survival of anuric peritoneal dialysis patients. Peritoneal dialysis international : journal of the International Society for Peritoneal Dialysis 2000;20(2):181-7.	: Sier QoL, men kun som psycological wellbeing and emotional stress
Biamino E, Caligaris F, Cesano G, Decostanzi E, Ferrero S, Imarisio P, et al. Morbidity and mortality in patients undergoing dialysis. Minerva urologica e nefrologica = The Italian journal of urology and nephrology 2000;52(3):127-8.	Time perspective (treatment periode 1992-1997)
Blake PG. Do mortality rates differ between hemodialysis and CAPD? A look at the Canadian vs. Dialysis and Transplantation 1996;25(2):75-100.	Not controlled study
Blake C, Codd MB, Cassidy A, O'Meara YM. Physical function, employment and quality of life in end-stage renal disease. Journal of nephrology 2000;13(2):142-9.	Wrong focus
Bose B, McDonald SP, Hawley CM, Brown FG, Badve SV, Wiggins KJ, et al. The effect of dialysis modality on the survival of end-stage renal disease patients with chronic hepatitis c infection - A multi-centre registry study. Nephrology 2011;Conference(var.pagings):73.	HD localization not specified
Brinker A, Haufe CC, Schumacher D, Braun N. Comparison of intermittent and continuous renal replacement therapy for acute renal failure in intensive care units of two major referral hospitals. NDT Plus 2010;Conference(var.pagings):iii52.	Acute renal failure
Brown EA, Johansson L, Farrington K, Gallagher H, Sensky T, Gordon F, et al. Broadening Options for Long-term Dialysis in the Elderly (BOLDE): differences in quality of life on peritoneal	Unclear HD localization

dialysis compared to haemodialysis for older patients. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2010;25(11):3755-63.	
Bugeja A, Dacouris N, Thomas A, Marticorena R, McFarlane P, Donnelly S, et al. In-center nocturnal hemodialysis: another option in the management of chronic kidney disease. Clinical journal of the American Society of Nephrology : CJASN 2009;4(4):778-83.	Compare conventional in-center HD with in-center thrice weekely nocturnal HD, ie both HD at the same place
Cafazzo JA, Leonard K, Easty AC, Rossos PG, Chan CT. Patient-perceived barriers to the adoption of nocturnal home hemodialysis. Clinical journal of the American Society of Nephrology : CJASN 2009;4(4):784-9.	Not our outcome (Barriers to adoption to nocturnal)
Cameron JI, Whiteside C, Katz J, Devins GM. Differences in quality of life across renal replacement therapies: A meta-analytic comparison. Am J Kidney Dis 2000;35(4):629-37.	Not our outcome, they say QoL, but only as psycological wellbeing and emotional stress
Carvounis CP, Manis T, Coritsidis G, Dubinsky M, Serpente P. Total lymphocyte count: A promising prognostic index of mortality in patients on CAPD. Perit Dial Int 2000;20(1):33-8.	Localization not specified for either PD or HD
Charra B, Terrat J-C, Vanel T, Chazot C, Jean G, Hurot J-M, et al. Long thrice weekly hemodialysis: The Tassin experience. Int J Artif Organs 2004;27(4):265-83. Ref ID: 3959	Time perspective (treatment periode 1968-2004) and analysing the results with a different focus than ours
Chauveau P, Larroumet N, Desvergenes C, Montoriol J, Combe C, Aparicio M. A 3-year prospective study of the outcome of patients dialyzed at home or in self-care units [abstract]. Nephrology Dialysis Transplantation 1999;14(9):A184.	Lack results
Choi SR, Lee SC, Kim BS, Yoon SY, Park HC, Kang SW, et al. Comparative study of renal replacement therapy in Korean diabetic end-stage renal disease patients: A single center study. Yonsei Med J 2003;44(3):454-62.	Time perspective (treatment periode 1986-1995)
Choi HY, Lee TW, Kim HC, Shin SK, Choi SO, Do JY, et al. Comparison of dialysis outcomes on hemodialysis (HD) vs. Nephrology 2010;Conference(var.pagings):37.	Sites not specified
Culleton BF, Walsh M, Klarenbach SW, Mortis G, Scott-	Compare conventional with nocturnal home. The problem is that the

Douglas N, Quinn RR, et al. Effect of frequent nocturnal hemodialysis vs conventional hemodialysis on left ventricular mass and quality of life: a randomized controlled trial. JAMA : the journal of the American Medical Association 2007;298(11):1291-9.	conventional group got their dialysis at different sites (in-center, self-care or home) and that the results are not specified.
Culleton BF, Walsh M, Klarenbach SW, Mortis G, Scott-Douglas N, Quinn RR, et al. Nocturnal hemodialysis lowers blood pressure and reduces left ventricular mass: results of a randomized controlled trial [abstract no: SU-FC002]. J Am Soc Nephrol 2007;18(Abstracts):67A-8A.	Abstract of the article above
Davenport A. How best to improve survival in hemodialysis patients: Solute clearance or volume control. Kidney Int 2011;80(10):1018-20.	Comment article
David S, Kumpers P, Eisenbach GM, Haller H, Kielstein JT. Prospective evaluation of an in-centre conversion from conventional haemodialysis to an intensified nocturnal strategy. Nephrology Dialysis Transplantation 2009;24(7):2232-40.	Compare conversion from conventional to intensified nocturnal, but at same center
de Jonge H, Bammens B, Lemahieu W, Maes BD, Vanrenterghem Y. Comparison of peritoneal dialysis and haemodialysis after renal transplant failure. Nephrology Dialysis Transplantation 2006;21(6):1669-74.	Wrong focus (after transplantation)
Fenton SS, Schaubel DE, Desmeules M, Morrison HI, Mao Y, Copleston P, et al. Hemodialysis versus peritoneal dialysis: a comparison of adjusted mortality rates. Am J Kidney Dis 1997;30(3):334-42.	Time perspective (treatment periode 1990-1994)
Fontan MP, Rodriguez-Carmona A, Falcon TG, Tresancos C, Rivera CF, Valdes F. Early predictors of survival in peritoneal dialysis and in-hospital hemodialysis. Nefrologia 1999;19(1):61-9.	Time perspective (treatment periode 1986-1997)
Fortes PC, Mendes JG, Sesiuk K, Marcondes LB, Aita CAM, Riella MC, et al. Glycemic and lipidic profile in diabetic patients undergoing dialysis. Arq Bras Endocrinol Metabol 2010;54(9):793-800.	Not our outcomes (glycemic and lipid profiles)
Frequent Hemodialysis Network (FHN) Trial Group. The Frequent Hemodialysis Network randomized trial of home nocturnal hemodialysis [abstract no: F-PO010]. J Am Soc Nephrol 2006;17(Abstracts):338A. Ref ID: 128 Abstract: ASN Annual Conference 14-19 November, 2006 -	No results

San Diego, CA, USA	
Frequent Hemodialysis Network (FHN) Trial Group. Progress of the frequent hemodialysis network randomized trial of in-center daily hemodialysis [abstract no: 61]. Am J Kidney Dis 2007;49(4):A40. Ref ID: 107 Abstract: National Kidney Foundation 2007 Spring Clinical Meetings, April 10-14 Florida	No results
Frequent Hemodialysis Network (FHN) Trial Group. The frequent hemodialysis network randomized trial of home nocturnal hemodialysis: change of trial design [abstract no: 62]. Am J Kidney Dis 2007;49(4):A40. Ref ID: 111 Abstract: National Kidney Foundation 2007 Spring Clinical Meetings, April 10-14 Florida	No results
Fu Y-J, Wang G-X, Huang Y-H. Hemodialysis and peritoneal dialysis associated with complications following renal transplantation: A restrospective analysis in 204 cases. Journal of Clinical Rehabilitative Tissue Engineering Research 2007;11(43):8637-40.	Sites not specified
Galland R, Traeger J. Short daily hemodialysis and nutritional status in patients with chronic renal failure. Seminars in Dialysis 2004;17(2):104-8.	Outcome (nutritional status) and site (some treated at home and some at self-care dialysis unit. The results were not specified)
Ganesh SK, Hulbert-Shearon T, Port FK, Eagle K, Stack AG. Mortality differences by dialysis modality among incident ESRD patients with and without coronary artery disease. J Am Soc Nephrol 2003;14(2):415-24.	Sites not specified
Gataa R, Ajmi TN, Haouala F, Mtiraoui A. Quality of life patterns of dialysed patients in the region of Kairouan. La Tunisie medicale 2008;86(1):68-74.	Design, not comparative
Gokal R, Figueras M, Olle A, Rovira J, Badia X. Outcomes in peritoneal dialysis and haemodialysis - A comparative assessment of survival and quality of life. Nephrology Dialysis Transplantation 1999;14(SUPPL. 6):24-30.	Overview, not SR
Goldstein A, Kliger AS, Finkelstein FO. Recovery of renal function and the discontinuation of dialysis in patients treated with continuous peritoneal dialysis. Perit Dial Int 2003;23(2):151-6.	Not our outcome

Gracia-Iguacel C, Gallar P, Qureshi AR, Ortega O, Mon C, Ortiz M, et al. Vitamin D deficiency in dialysis patients: Effect of dialysis modality and implications on outcome. J Ren Nutr 2010;20(6):359-67.	The outcome survival do not specify the results for hemofiltration and conventional HD
Gracia C, Gallar P, Quresi AR, Ortega O, Sanchez M, Callejas R, et al. Vitamin D deficiency in dialysis patients: Impact of dialysis modality and implications on outcome. Blood Purif 2009;Conference(var.pagings):319.	Abstract to the article above
Greene T, Daugirdas JT, Depner TA, Gotch F, Kuhlman M. Solute Clearances and Fluid Removal in the Frequent Hemodialysis Network Trials. Am J Kidney Dis 2009;53(5):835-44.	Not our outcome (Dialyse dose)
Griva K, Davenport A, Harrison M, Newman S. An evaluation of illness, treatment perceptions, and depression in hospital- vs. J Psychosom Res 2010;69(4):363-70.	Not our outcome
Harris SAC, Lamping DL, Brown EA, Constantinovici N, Phillips M, Barnes G, et al. Clinical outcomes and quality of life in elderly patients on peritoneal dialysis versus hemodialysis. Perit Dial Int 2002;22(4):463-70.	Results not specified
Heidenheim AP, Muirhead N, Moist L, Lindsay RM. Patient quality of life on quotidian hemodialysis. American journal of kidney diseases : the official journal of the National Kidney Foundation 2003;42(1 Suppl):36-41.	Site for the comparator (conventional HD) can be both home, satellite and hospital-without specifying the results
Hiroshige K, Yuu K, Soejima M, Takasugi M, Kuroiwa A. Rapid decline of residual renal function in patients on automated peritoneal dialysis. Perit Dial Int 1996;16(3):307-15.	Time perspective (treatment periode 1992-94)
Hirsch DJ, Jindal KK, Schaubel DE, Fenton SS. Peritoneal dialysis reduces the use of non native fistula access in dialysis programs. Adv Perit Dial 1999;Conference on Peritoneal Dialysis. 15(pp 121-124):-124.	Time perspective (treatment periode 1990-1996)
Holland DC, Meers C, Lawlor ME, Lam M. Serial prealbumin levels as predictors of outcomes in a retrospective cohort of peritoneal and hemodialysis patients. Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation 2001;11(3):129-38.	Results not specified
Jaber BL, Finkelstein FO, Glickman JD, Hull AR, Kraus MA, Leypoldt JK, et al. Scope and Design of the Following Rehabilitation, Economics and Everyday-Dialysis Outcome Measure-	Study protocol

ments (FREEDOM) Study. Am J Kidney Dis 2009;53(2):310-20.	
Janda K, Stompor T, Gryz E, Szczudlik A, Drozdz M, Krasniak A, et al. Evaluation of polyneuropathy severity in chronic renal failure patients on continuous ambulatory peritoneal dialysis or on maintenance hemodialysis. Przegl Lek 2007;64(6):423-30.	Not our outcome
Jankovic N, Orsanic-Brcic D, Nadinic-Safar B, Pavlovic D, Varlaj-Knobloch V, Cala S, et al. Dialysis adequacy of our patients in comparison with NKF-DOQI clinical practice guidelines. Periodicum Biologorum 2000;102(1):99-101.	Not our outcome
Jefferies HJ, Virk B, Schiller B, Moran J, McIntyre CW. Frequent hemodialysis schedules are associated with reduced levels of dialysis-induced cardiac injury (myocardial stunning). Clinical Journal of the American Society of Nephrology 2011;6(6):1326-32.	Not our outcome
Juergensen E, Wuerth D, Finkelstein SH, Juergensen PH, Bekui A, Finkelstein FO. Hemodialysis and peritoneal dialysis: patients' assessment of their satisfaction with therapy and the impact of the therapy on their lives. Clinical journal of the American Society of Nephrology : CJASN 2006;1(6):1191-6.	Not our outcome
Kobus G, Malyszko J, Mysyliwiec M. [Cardiovascular risk factors in dialyzed patients]. Pol Arch Med Wewn 2004;112(6):1425-31.	Do not know sites or treatment periode
Koch M, Kutkuhn B, Grabensee B, Ritz E. Apolipoprotein A, fibrinogen, age, and history of stroke are predictors of death in dialysed diabetic patients: A prospective study in 412 subjects. Nephrology Dialysis Transplantation 1997;12(12):2603-11.	Time perspective (treatment periode 1985-1994)
Koch M, Kohnle M, Trapp R, Haastert B, Rump LC, Aker S. Comparable outcome of acute unplanned peritoneal dialysis and haemodialysis. Nephrology Dialysis Transplantation 2012;27(1):375-80.	The population includes patients with acute renal failure
a Y, Takahara S, Miyake O, Nonomura N, Morimoto A, Mori H. Renal cell carcinoma in dialysis patients: A single center experience. Int J Urol 2006;13(8):1045-8.	Results not specified
Kraus M, Burkart J, Hegeman R, Solomon R, Coplon N, Moran J. A comparison of center-based vs. home-based daily hemodialysis for patients with end-stage renal disease. Hemodialysis International 2007;11(4):468-77.	Cross over
Kumano, K; Kawaguchi, Y. Multicenter cross-sectional study	Not our outcomes (dialysisdose and

for dialysis dose and physician's subjective judgment in Japanese peritoneal dialysis patients. Am J Kidney Dis 2000;35(3):515-25.	nutritional state)
Kutner NG, Zhang R, McClellan WM, Cole SA. Psychosocial predictors of non-compliance in haemodialysis and peritoneal dialysis patients. Nephrology Dialysis Transplantation 2002;17(1):93-9.	No results, sites not specified
Lang SM, Bergner A, Topfer M, Schiffl H. Preservation of residual renal function in dialysis patients: effects of dialysis-technique-related factors. Perit Dial Int 2001;21(1):52-7.	Not our focus
Lankisch PG, Weber-Dany B, Maisonneuve P, Lowenfels AB. Frequency and severity of acute pancreatitis in chronic dialysis patients. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2008;23(4):1401-5.	Sites for HD unclear
Law MC, Fung JSF, Chow KM, Szeto CC, Li PKT. Hong Kong continuous ambulatory peritoneal dialysis patients reported health-related quality of life comparable to hemodialysis patients in developed countries. Hemodialysis International 2009;Conference(var.pagings):380.	Unclear sites (compare PD in Hong Kong with HD in Europe. In Hong one renal unit?, sites in Europe unknown)
Leitch R, Ouwendyk M, Ferguson E, Clement L, Peters K, Heidenheim AP, et al. Nursing issues related to patient selection, vascular access, and education in quotidian hemodialysis. American journal of kidney diseases : the official journal of the National Kidney Foundation 2003;42(1 Suppl):56-60.	This i s the London Daily/Nocturnal Hemodialysis Study Ikke på listen. This is the same population as for Heidenheim (above), ie Site for the comparator (conventional HD) can be both home, satellite and hospital- without specifying the results
Liem YS, Wong JB, Hunink MGM, De Charro FT, Winkelmayer WC. Comparison of hemodialysis and peritoneal dialysis survival in The Netherlands. Kidney Int 2007;71(2):153-8.	Not appropiate design
Lim YN, Lim TO, Lee DG, Wong HS, Ong LM, Shaariah W, et al. A report of the Malaysian dialysis registry of the National Renal Registry, Malaysia. Med J Malaysia 2008;63(SUPPL. C):5-8.	Localization for HD uncertain
Lim KB, Ma V, Lee EJC. Pulmonary hypertension in chronic kidney disease 3 in a multiethnic asian population. Hemodialysis International 2009;Conference(var.pagings):397-8.	Localization uncertain. Abstract
Lindsay RM, Leitch R, Heidenheim AP, Kortas C, London Daily/Nocturnal Hemodialysis Study. The London Daily/Nocturnal	Results not specified for the different sites

Hemodialysis Study--study design, morbidity, and mortality results. American journal of kidney diseases : the official journal of the National Kidney Foundation 2003;42(1 Suppl):5-12.	
Lobbedez T, Lecouf A, Ficheux M, Henri P, De Ligny BH, Ryckelynck J-P. Is rapid initiation of peritoneal dialysis feasible in unplanned dialysis patients? A single-centre experience. Nephrology Dialysis Transplantation 2008;23(10):3290-4.	Localization uncertain
MacRae JM, Rose CL, Jaber BL, Gill JS. Utilization and outcome of 'out-of-center hemodialysis' in the United States: A contemporary analysis. Nephron - Clinical Practice 2010;116(1):c53-c59.	Results for hospital and satellite are combined
Maiorca R, Cancarini G, Brunori G, Zubani R, Camerini C, Manili L, et al. Which treatment for which patient in the future? Possible modifications in CAPD. Nephrology Dialysis Transplantation 1995;10(SUPPL. 7):20-6.	Time perspective (treatment periode 1981-1993)
Maiorca R, Cancarini GC, Zubani R, Camerini C, Manili L, Brunori G, et al. CAPD viability: A long-term comparison with hemodialysis. Perit Dial Int 1996;16(3):276-87.	Time perspective (treatment periode 1981-1993)
Maiorca R, Cancarini GC, Brunori G, Zubani R, Camerini C, Manili L, et al. Comparison of long-term survival between hemodialysis and peritoneal dialysis. Adv Perit Dial 1996;Conference on Peritoneal Dialysis. 12(pp 79-88):-88.	Time perspective (treatment periode 1981-1993)
Manns BJ, Klarenbach S, Walsh M, Quinn R, Tonelli M, Scott-Douglas N, et al. The impact of nocturnal hemodialysis on quality of life: results of a randomized controlled trial [abstract no: F-PO891]. J Am Soc Nephrol 2007;18(Abstracts):298A-9A.	Sites not given. Abstract
Marshall MR, Hawley CM, Kerr PG, Polkinghorne KR, Marshall RJ, Agar JWM, et al. Home hemodialysis and mortality risk in Australian and New Zealand populations. Am J Kidney Dis 2011;58(5):782-93.	Sites not specified (Hospital and satellite in one group, and home and community house in one group)
McDonald SP, Marshall MR, Johnson DW, Polkinghorne KR. Relationship between dialysis modality and mortality. J Am Soc Nephrol 2009;20(1):155-63.	Do not know HD localization
McGregor DO, Buttimore AL, Lynn KL, Nicholls MG, Jardine DL. A Comparative Study of Blood Pressure Control with Short In-Center versus Long Home Hemodialysis. Blood Purif 2001;19(3):293-300.	Not our outcome (BP)

Merkus MP, Jager KJ, Dekker FW, Boeschoten EW, Stevens P, Krediet RT, et al. Quality of life in patients on chronic dialysis: Self-assessment 3 months after the start of treatment. Am J Kidney Dis 1997;29(4):584-92.	Time perspective (treatment periode 1983-1995)
Merkus MP, Jager KJ, Dekker FW, De Haan RJ, Boeschoten EW, Krediet RT. Physical symptoms and quality of life in patients on chronic dialysis: Results of the Netherlands Cooperative Study on Adequacy of Dialysis (NECOSAD). Nephrology Dialysis Transplantation 1999;14(5):1163-70.	Time perspective (treatment periode 1983-1995)
Merkus MP, Jager KJ, Dekker FW, De Haan RJ, Boeschoten EW, Krediet RT. Quality of life over time in dialysis: The Netherlands cooperative study on the adequacy of dialysis. Kidney Int 1999;56(2):720-8.	Time perspective (treatment periode 1983-1995)
Moreno F, Lopez Gomez JM, Sanz-Guajardo D, Jofre R, Valderrabano F. Quality of life in dialysis patients. Nephrology Dialysis Transplantation 1996;11(SUPPL. 2):125-9.	Treatment periode 1993
Nesrallah G, Suri R, Moist L, Kortas C, Lindsay RM. Volume control and blood pressure management in patients undergoing quotidian hemodialysis. American journal of kidney diseases : the official journal of the National Kidney Foundation 2003;42(1 Suppl):13-7.	Not our outcome (volume controll BP)
Nesrallah GE, Lindsay RM, Cuerden MS, Garg AX, Port F, Austin PC, et al. Intensive hemodialysis associates with improved survival compared with conventional hemodialysis. J Am Soc Nephrol 2012;23(4):696-705.	Unclear localization
Nthite T, Swanepoel C, Arendse C, Okpechi I. Peritoneal dialysis as a dialysis option for emerging countries: Perspectives from a quality-of-life (QOL) study in Cape Town. Cardiovascular Journal of Africa 2010;Conference(var.pagings):S12-June.	This article (supplement) could not be obtained from the library
Oliver MJ, Verrelli M, Zacharias JM, Blake PG, Garg AX, Johnson JF, et al. Choosing peritoneal dialysis reduces the risk of invasive access interventions. Nephrology Dialysis Transplantation 2012;27(2):810-6.	Unclear localization for HD
Osthus TBH, Sandvik L, Dammen T, Leivestad T, Os I. Quality of life predicts mortality in dialysis patients. NDT Plus 2010;Conference(var.pagings):iii102.	Not our outcome

Overgaard CB, Chowdhary S, Zur RL, Bui S, Wainstein R, Barolet AW, et al. Comparison of coronary vasoreactivity in endstage renal disease patients receiving conventional intermittent vs. Can J Cardiol 2011;Conference(var.pagings):S114-October.	Not our focus
Page DE, Lavoie SL, Knoll GA. Team approach in a peritoneal dialysis unit provides better control of hypertension than in a hemodialysis unit. Adv Perit Dial 2004;20:117-20.	Not our outcome (BP)
Pauly RP, Asad RA, Hanley JA, Pierratos A, Zaltzman J, Chery A, et al. Long-term clinical outcomes of nocturnal hemodialysis patients compared with conventional hemodialysis patients post-renal transplantation. Clin Transplant 2009;23(1):47-55.	Wrong focus (post-renal transplantation). Sites unkown
Pauly RP. Nocturnal Home Hemodialysis and Short Daily Hemodialysis Compared With Kidney Transplantation: Emerging Data in a New Era. Advances in Chronic Kidney Disease 2009;16(3):169-72.	Design. Overview, not SR
Peres LAB, Biela R, Herrmann M, Matsuo T, Ann HK, Camargo MTA, et al. [Epidemiological study of end-stage kidney disease in western Parana. Jornal Brasileiro de Nefrologia 2010;32(1):49-54.	The data analysis did not specify the different population groups. Time perspective (treatment periode 1984-2009)
Perez Garcia R, Rodriguez Benitez P, Dall'Anesse C, Gomez Campdera F, Valderrabano F. [Pre-occupying increase in diabetes as cause for terminal kidney failure. An Med Interna 2001;18(4):175-80.	Time perspective (treatment periode 1978-1998)
Piraino B, Sheth H. Peritonitis - Does peritoneal dialysis modality make a difference? Blood Purif 2010;29(2):145-9.	Design. Overview, not SR
Plantinga LC, Fink NE, Harrington-Levey R, Finkelstein FO, Hebah N, Powe NR, et al. Association of social support with outcomes in incident dialysis patients. Clinical Journal of the American Society of Nephrology 2010;5(8):1480-8.	Not our outcome (association between social support and outcomes)
Ricka R, Evers GC. The manner of care, self care and quality of life dialysis patients. Pflege 2004;17(1):15-21.	Not our outcome
Rocco MV, Larive B, Eggers PW, Beck GJ, Chertow GM, Levin NW, et al. Baseline characteristics of participants in the Frequent Hemodialysis Network (FHN) daily and nocturnal trials.	Only baseline characteristica

American journal of kidney diseases : the official journal of the National Kidney Foundation 2011;57(1):90-100.	
Rocco MV, Lockridge J, R.S, Beck GJ, Eggers PW, Gassman JJ, et al. The effects of frequent nocturnal home hemodialysis: The Frequent Hemodialysis Network Nocturnal Trial. Kidney Int 2011;80(10):1080-91.	Compare to different HD, but both at home
Rodriguez-Carmona A, Fontan MP, Falcon TG, Rivera CF, Valdes F. A comparative analysis on the incidence of peritonitis and exit-site infection in CAPD and automated peritoneal dialysis. Perit Dial Int 1999;19(3):253-8.	Time perspective (treatment periode 1989-1998)
Rojas L, Mnoz P, Kestler M, Arroyo D, Rodriguez-Creixems M, Verde E, et al. Bloodstream infection in patients with kidney disease. Clinical Microbiology and Infection 2011;Conference(var.pagings):S415.	Lack control group
Ross S, Dong E, Gordon M, Connelly J, Kvasz M, Iyengar M, et al. Meta-analysis of outcome studies in end-stage renal disease. Kidney International, Supplement 2000;57(74):S28-S38.	Design (meta-analyse), time period (most of the articles after 1988), do not know sites
Russo GE, Morgia A, Cavallini M, Centi A, Broccoli ML, Cicchinelli A, et al. Quality of life assessment in patients on hemodialysis and peritoneal dialysis. Giornale italiano di nefrologia : organo ufficiale della Societa italiana di nefrologia 2010;27(3):290-5.	Do not know site for HD
Sands JJ, Lacson J, E, Ofsthun NJ, Kay JC, Diaz-Buxo JA. Home hemodialysis: A comparison of in-center and home hemodialysis therapy in a cohort of successful home hemodialysis patients. ASAIO J 2009;55(4):361-8.	Cross over (data only for the total group)
Saner E, Nitsch D, Descoeudres C, Frey FJ, Uehlinger DE. Outcome of home haemodialysis patients: A case-cohort study. Nephrology Dialysis Transplantation 2005;20(3):604-10.	Time perspective (treatment periode 1970-1995)
Schwartz DI, Pierratos A, Richardson RMA, Fenton SSA, Chan CT. Impact of nocturnal home hemodialysis on anemia management in patients with end-stage renal disease. Clin Nephrol 2005;63(3):202-8.	Not our outcome (anemia)
Selgas R, Cirugeda A, Fernandez-Perpen A, Sanchez-Tomero JA, Barril G, Alvarez V, et al. Comparisons of hemodialysis and CAPD in patients over 65 years of age: a meta-analysis. Int Urol Nephrol 2001;33(2):259-64.	Design (Meta-analyse). We have checked the included articles from 1995 and after. We already have the actual ones

Sitter T, Krautz B, Held E, Schiffl H. [Patient survival, a change in methods, and hospitalization in CAPD abd hemodialysis]. Deutsche medizinische Wochenschrift (1946) 1997;122(5):109-15.	Time perspective (treatment periode 1987-1992)
Soleymanian T, Raman S, Shannaq FN, Richardson R, Jassal SV, Bargman J, et al. Survival and morbidity of HIV patients on hemodialysis and peritoneal dialysis: One center's experience and review of the literature. Int Urol Nephrol 2006;38(2):331-8.	Do not know localization
Spanner E, Suri R, Heidenheim AP, Lindsay RM. The impact of quotidian hemodialysis on nutrition. American journal of kidney diseases : the official journal of the National Kidney Foundation 2003;42(1 Suppl):30-5.	Not our outcome (nutrition)
Srivaths P, Rajesh K, Lori B, Bennett M, Qing M, Christopher H, et al. Cardiac Calcifications (CC) are more prevalent in Hemodialysis (HD) when compared to Peritoneal Dialysis (PD) Pediatric (ped) end-stage renal disease (ESRD) patients (pts). Perit Dial Int 2012;Conference(var.pagings):S24.	Children
Stack AG, Molony DA, Rahman NS, Dosekun A, Murthy B. Impact of dialysis modality on survival of new ESRD patients with congestive heart failure in the United States. Kidney Int 2003;64(3):1071-9.	Do not know sites
Susantitaphong P, Koulouridis I, Balk EM, Madias NE, Jaber BL. Effect of frequent or extended hemodialysis on cardiovascular parameters: A meta-analysis. Am J Kidney Dis 2012;59(5):689-99.	Do not know localization for HD
Tang YL, Leung KCD. Impacts on quality of life in end-stage renal disease patients on chronic hemodialysis in hospital-based and community-based hemodialysis center settings. Hemodialysis International 2009;Conference(var.pagings):427-8.	Chinese version of KDQL
Theofilou PA. Sexual functioning in chronic kidney disease: The association with depression and anxiety. Hemodialysis International 2012;16 (1):76-81.	Not or outcome (sexual function)
Theofilou P. Quality of life and mental health in hemodialysis and peritoneal dialysis patients: the role of health beliefs. Int Urol Nephrol 2012;44(1):245-53.	Not our outcome (health beliefs)
Trbojevic J, Nesic D, Stojimirovic B. Effect of various methods of treatment in chronic renal insufficiency on the quality of life in patients. Srp Arh Celok Lek 1998;126(9-10):374-8.	Localization not known

Tse K-C, Lui S-L, Lo W-K. Comparison of long-term survical (beyond 12 years) in patients on peritoneal dialysis and on hemodialysis. Perit Dial Int 2003;23(SUPPL. 2):S104-S108.	Treatment period started 1990
Ur-Rehman K, Housawi A, Al-Jifri A, Kielar M, Al-Ghamdi SM. Peritoneal dialysis for chronic kidney disease patients: a single-center experience in Saudi Arabia. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia 2011;22(3):581-6.	Lack control
Van Eps CL, Jones M, Ng T, Johnson DW, Campbell SB, Isbel NM, et al. The impact of extended-hours home hemodialysis and buttonhole cannulation technique on hospitalization rates for septic events related to dialysis access. Hemodialysis International 2010;14(4):451-63.	Two types of HD (different frequences), but both at home
Vos PF, Zilch O, Jennekens-Schinkel A, Salden M, Nuyen J, Kooistra MMP, et al. Effect of short daily home haemodialysis on quality of life, cognitive functioning and the electroencephalogram. Nephrology Dialysis Transplantation 2006;21(9):2529-35.	No control group for our outcomes
Walsh M, Manns BJ, Klarenbach S, Quinn R, Tonelli M, Culleton BF. The effects of nocturnal hemodialysis compared to conventional hemodialysis on change in left ventricular mass: Rationale and study design of a randomized controlled pilot study. BMC nephrology.	Study protocol
Weinhandl E, Liu J, Gilbertson D, Arneson T, Collins A. Relative mortality in daily home and matched, thrice-weekly in-center hemodialysis patients. Am J Kidney Dis 2011;Conference(var.pagings):A103.	Abstract of Weinhandl 2012 that we have included
Wight JP, Edwards L, Brazier J, Walters S, Payne JN, Brown CB. The SF36 as an outcome measure of services for end stage renal failure. Qual Health Care 1998;7(4):209-21.	Only analyses of the total group
Winkelmayer WC, Glynn RJ, Mittleman MA, Levin R, Pliskin JS, Avorn J. Comparing mortality of elderly patients on hemodialysis versus peritoneal dialysis: a propensity score approach. Journal of the American Society of Nephrology : JASN 2002;13(9):2353-62.	Time perspective (treatment periode 1991-1996). Unclear HD localization
Wyld M, Morton R, Hayen A, Howard K, Webster A. A meta-	Meta-analyse. Do not separate the

analysis of quality of life estimates in chronic kidney disease. Nephrology 2010;Conference(var.pagings):33.	results for the PD and HD groups at home
Young B, Sevinc E, Rigodanzo-Massey N, Blagg C. Mortality differences by modality among home hemodialysis patients. Hemodialysis International 2010;Conference(var.pagings):126.	Compare different HD, but all at home

Table III: *The manual search from websites of other HTA agencies resulted in the following articles from CADTH and Dacehta that we have reviewed and excluded*

Study First author (reference no.)	Cause for exclusion of study
From CADTH (The Canadian Agency for Drugs and Technologies in Health) Evidence in Context from 2008. Barret et al. The Provision of Dialysis Services in Rural and Remote populations in Newfoundland and Labrador.	Not according to our PICO, but we checked 3 of the primary studies from this: (Greneche 2005: not relevant due to design; Walsh 2005: no control group and Lee 2002: not our outcome)
From Dacetha: Sundhedsstyrelsen, Center for Evaluering og Medicinsk Teknologivurdering Dialyse ved kronisk nyresvigt – kan antallet af patienter i udgående dialyse øges? En medicinsk teknologivurdering København: Sundhedsstyrelsen, Center for Evaluering og Medicinsk Teknologivurdering, 2006 Medicinsk Teknologivurdering 2006; 8(3)	<u>*Center HD vs home HD*</u> They included: *2 SR:* Mowatt 2004: Our search included Mowatt 2004, this we have excluded of reasons given above in table 1. Jacobs 1995: Our search did not include this. We have checked and found that the study period here was before 1995, ie out. *3 original studies* comparing mortalitet between CHD and HHD: Mailoux LU 1996 (this is not in our interest since the study period from 1970 through 1993) Woods 1996 (this we had in our search, but we have excluded since treatment period from 1986-87) Arkouche 1999 (this we had in our search, but we have excluded since treatment period from 1974-97) <u>*Center HD vs selfcare HD in center*</u> Here they found no literature. <u>*Center HD vs home PD (APD og CAPD)*</u>

	1 RCT: Korevaar 2003. This we have already included.. Observational studies: Bloembergen 1995: this we did not have, we have checked, out due to the treatment period from 1974-97; Ganesh 2003: this we already have from our search; excluded due to lack of localization Stack 2003: this we already have from our search; excluded due to lack of localization Jaar 2005: this we did not have, we have checked this and we include this as one of our two articles from manual search. Later we found that the patient groups in this study differ significantly in comorbidity between groups, and hence we have only mention this in our Appendix. Vonesh 2004: this we did not have, we have checked, this is not of our interest due to unkown localization. Fenton 1997: This we had in our search, excluded due to treatment period 1990-94. Schaubel 1998: This we did not have in our search. Have checked, exclude due to treatment period 1990-95 Collins 1999: This we did not have in our search. Have checked, exclude due to treatment period 1994-96 and localization not stated Heaf 2002: This is a Danish register study from 1990-99. This we have excluded both since we do not know the site(s) for HD. ie: we exclude the Danish MTV, since we either had already their studies, or their studies were not of our interest, except for one study (Jaar) that we have added as an manual searched article in our HTA.

Appendix 3- Studies not assessed due to either lack of comorbidity data or significant difference in comorbidity data between the patient groups

Author, year/ study type	Number of patients (total in study)	Outcome(s)	Lack of comorbidity Data	Significant difference in comorbidity	Comments
PD versus HD hospital					
Bayoumi, 2010 (80)	200	QoL	X		No adjustment for comorbidity in analyses.
De Mutsert, 2009 (81)	700	Mortality		X	High risk of comorbidity (according to comorbidity score of Khan et al), p=0.001. Adjusted analyses did not address the relevant comparison (PD versus HD hospital).
Tchokhonelidze 2007(82)	305	Mortality		X	Total comorbidity, p<0.001; diabetes, p=0.005. Adjusted analyses only partially adjust for baseline differences (adjusted for diabetes but not for total comorbidity).
Wasserfallen, 2004 (83)	622	QoL	X		No adjustment for comorbidity in analyses.
Enriquez, 2005 (84)	236	Mortality	X		No adjustment for comorbidity in analyses.
Erkoc, 2004 (85)	287	Complications	X		No adjustment for comorbidity in analyses.
Ginieri-Coccossis, 2008 (86)	144	QoL	X		No adjustment for comorbidity in analyses.

Niu, 2005 (87)	160	QoL	X		No adjustment for comorbidity in analyses.
Theofilou, 2011 (88)	144	QoL	X		No adjustment for comorbidity in analyses.
Uchida, 2007 (89)	574	Mortality		X	Diabetes significant different . Adjusted analyses for diabetic versus non-diabetic patients could have allowed us to treat these groups as separate studies, but it was no longer possible to determine whether baseline characteristics were identical between the new groups.
HD satellite versus HD hospital					
Bernstein, 2010(90)	2663	Mortality	X		No adjustment for comorbidity in analyses.
Nitsch, 2011 (91)	1048	Mortality	X		No comorbidity data, except that blood pressure was similar across groups. No adjustment for comorbidity in analyses.
HD home versus HD hospital					
Nitsch, 2011 (91)	1048	Mortality	X		No comorbidity data, except that blood pressure was similar across groups. No adjustment for comorbidity in

					analyses.
PD home versus HD satellite					
Kutner, 2005 (92)	868	Mortality, QoL		X	Cardiovascular comorbidity significant different. (Blood pressure,ns). No adjustment for comorbidity in analyses.
Nitsch, 2011 (91)	988	Mortality	X		No comorbidity data, except that blood pressure was similar across groups. No adjustment for comorbidity in analyses.
Jaar, 2005 (63)	1041	Mortality		X	Index of Coexistent Disease Score, cardio-vascular disease, significant different. Performed adjusted analyses, but did not adjust for all factors that were different between groups at baseline (no explanation as to why).
HD home versus HD satellite					
Nitsch, 2011 (91)	471	Mortality	X		No comorbidity data, except that blood pressure was similar across groups. No adjustment for comorbidity in analyses.
HD home versus PD home					
Nitsch, 2011 (91)	895	Mortality	X		No comorbidity data, except that blood pressure was similar across groups. No adjustment for comorbidity in

				analyses.
APD versus CAPD				
Barone, 2005 (93)	73	Complications	X	Baseline characteristics were not specified for the groups
Petrakis, 2010/ Retrospective cohort (94)	20	Mortality, complications	X	No adjustment for comorbidity in analyses.
Su, 2010 (95)	172	Complications	X	No adjustment for comorbidity in analyses.

Appendix 4- Patient characteristics at baseline

Table I: *Patient characteristics at baseline for the studies assessed for PD home vs HD hospital*

Author year/ Study period	Patient characteristics at baseline	INTERVENTION PD	CONTROL HD hospital
Korevaar 2003(19) / 1997-2000	Total number of patients (N) Mean age % male *Comorbidity* Khans comorbidity score(%) Low Medium High *Primary kidney disease* (%) Diabetes Glomerulonephritis Renal vascular disease *Incident or established patients*	N=20 55±12 55 45 35 20 20 15 15 Incident	N=18 62±11, p* 61, p= 0.84** 50 22 28, p=0.66*** 28 0 22 Incident
Andrikos 2008(12) / 1995-2000	Total number of patients (N) Mean age	N=48 55±18	N=46 54±16, p=0.57

	% male *Comorbidity (%)* Coronary heart disease Diabetes Hypertension Dyslipedemi COPD Peripher vascular disease *Primary kidney disease (%)* *Incident or established patients*	55 21 19 85 33 6 15 Not reported Incident	48, p=0.73 22, p=0.90 13, p=0.45 80, p=0.52 20, p=0.06 11, p=0.25 17, p=0.63 Not reported Incident
Ganeshadeva 2009(16) / Jan 2007-Dec 07	Total number of patients (N) Mean age % male *Comorbidity (%)* Diabetics Ischaemic Heart Disease Hypertension *Primary kidney disease (%)* Previous cerebrovascular accident *Incident or established patients*	N=63 52±15 38 62 19 87 5 Both	N=74 53±15, p=0.630 67, p=0.001 48, p=0.103 26, p=0.312 82, p=0.411 8 Both
Jager 2001(17) / 1994-95	Total number of patients (N) Mean age % male *Comorbidity (%)* Diabetes mellitus Malignancy Cerebrovascular accident Cardiovascular disease Ischaemic heart disease Angina pectoris Myocardial infarction Congestive heart failure (NYHA III/IV)	N=118 54±14 64 20 3 8 25 14 10 9 4	N=132 59±16, p<0.01 53, p=ns 17, p=ns 9, p<0.05 8, p=ns 30, p=ns 15, p=ns 11, p=ns 10, p=ns 6, p=ns

	Peripheral vascular disease	15	18, p=ns
	Davies risk score		
	no comorbidity	53	46, p=ns
	intermediate	41	47, p=ns
	severe comorbidity	7	7, p=ns
	Systolic blood pressure	143	148, p<0.05
	Diastolic blood pressure	85	81, p<0.05
	Primary kidney diseas (%)		
	Renal vascular disease	23	23
	Diabetes mellitus 16	16	14
	Glomerulonephritis 16	16	9
	Incident or established patients	Incident	Incident
Lee 2008(21) / 2002-05	Total number of patients (N)=190	N=190	N=344
	% of patients ≥60 years***	60	45, ns difference**
	% male***	50	62, ns difference**
	Comorbidity (%)		
	Diabetes***	69	65, ns difference**
	Primary kidney diseas (%)	Not reported	Not reported
	Incident or established patients	Incident patients	Incident patients
Ruiz Retana 2009 (23)/?	Total number of patients (N)	N=32	N=61
	Mean age	49.6±14.0	55.8±9.6, p=0.032
	% male	53	26, p=0.01
	Comorbidity		
	Charlson index score	1.79 (1.07-2.50)	1.94 (1.43-1.79), p≤0.65
	Primary kidney disease (%)	Not reported	Not reported
	Incident or established patients	Both	*Both*
Zhang 2007 (29) /2004-05*****	Total number of patients (N)	N=408	N=654
	Mean age	61.6±12.7	57.2 ±12.5, p<0.001**
	% male	40.4	55.0, p=0.006**
	Comorbidity		
	Charlson index score	4.30±0.58	4.78±1.06, p<0.001**
	Primary kidney disease		

	(%) Glomerulonephritis Hypertensive nephropathy Diabetic nephropathy *Incident or established patients*	 47.8 15.4 10.2 ?	46.0 16.8 15.1 ?
Verdalles 2010(25) / 2000-07	Total number of patients (N) Mean age % male *Comorbidity* Charlson index score *Primary kidney disease (%)* *Incident or established patients*	 N=11 79.4±4.5 54.5 9.4±1.8 Not reported Incident	 N=128 78.5±2.4, p= 0.267 57.0, p=0.713 10±1.8, p=0.260 Not reported Incident
Vigneau 2000(26) / 1994-97	Total number of patients (N) Mean age % male *Comorbidity* Cardiovascular complications Coronary Cardiac failure *Primary kidney disease (%)* *Incident or established patients*	 N=14**** 70.2±3.4 43 5 2 Not reported Incident	 N=14**** 65.0±3.6, p=ns 35, p=ns p=ns 2 1 Not reported Incident

* P-value for age could not be calculated (too little data)

** The p-values calculated by us

*** The data are taken from a bar diagram, so values are approximate

**** All were type II diabetes patients

*****Included, even though significant difference in comorbidtity between groups, since the analysis for quality of life was adjusted for this

Table II: *Patient characteristics at baseline for the study assessed for HD satellite versus HD hospital*

Author year/ Study period	Patient characteristics at baseline	INTERVENTION HD satellite	CONTROL HD hospital
Roderick 2005(22) / 2000-2001	Total number of patients (N)	N=394	N=342
	Mean age	62.48±16.11	56.55±17.56, p<0.001
	% male	63.5	60.8, p=0.462
	Comorbidity		
	Wright/Khan comorbidity index (%)		
	Low	29.5	36.3, p=0.152
	Medium	37.4	35.3
	High	33.1	28.4
	Comorbidtity score-Lister (%)		
	None	48.4	52.2, p=0.124
	Mild/moderate: 38.0	38.0	39.1
	Severe	13.7	8.8
	Comorbidity score-modified Charlson (%)		
	Low	58.2	62.2, p=0.285
	Moderate	23.8	24.7
	High	11.7	7.5
	Very high	6.3	5.6
	Primary kidney disease (%)		
	Other	61.4	60.9, p=0.885
	Primar renal disease	38.6	39.1
	Incident or established patients	Established	Established

Table III: *Patient characteristics at baseline for the studies assessed for PD home versus HD satellite*

Author year/ Study period	Patient characteristics at baseline	INTERVENTION PD	CONTROL HD satellite
Aslam 2006 (13)/ 1999-2005	Total number of patients (N)	N=62	N=119
	Mean age	55±17	59±16, p=0.15
	% male	44	57, p=0.12

	Comorbidity (%) Diabetes Charlson comorbidity index, median (range): *Primary kidney disease (%)* *Incident or established patients*	 46 6 (2-14) Not reported Incident	 54 p=0.35 6(2-14), p= 0.23 Not reported Incident
Williams 2011 (23)/ 2004-08	Total number of patients (N) Mean age % male *Comorbidity (%)* Diabetes Coronary artery disease Congestive heart failure Other cardiac diseases Peripheral vascular disease Cerebral vascular disease Cancer *Primary kidney disease (%)* *Incident or established patients*	 N=71 67±14 59 51 39 23 27 10 17 10 Not reported Incident	 N=97 67±17 69 41, p=0.27 39, p=1 30, p=0.52 28, p=0.68 21, p=0.17 14, p=0.88 18, p=0.25 Not reported Incident

Table IV: *Patient characteristics at baseline for the studies assessed for HD home versus HD satellite*

Author year/ Study period	Patient characteristics at baseline	INTERVENTION HD home	CONTROL HD satellite
Johansen 2008, NHD (18)/ 1997-2006	Total number of patients (N) Mean age % male *Comorbidity (%)* Congestive heart failure:	 N=94 47.0±16.3 64.9 17.9	 N=940 46.7±17.5, p=0.87 66.0, p=0.84 23.6, p=0.24

	Coronary artery disease Cerebral vascular disease Peripher vascular disease Diabetes *Primary kidney disease (%)* *Incident or established patients*	23.8 7.1 6.0 27.4 Not reported Established	17.4, p=0.14 5.0, p=0.39 10.3, p=0.20 28.3, p=0.85 Not reported Established
Johansen 2008, SDHD (18)/ 1997-2006	Total number of patients (N) Mean age % male *Comorbidity (%)* Congestive heart failure Coronary artery disease Cerebral vascular disease Peripher vascular disease Diabetes *Primary kidney disease (%)* *Incident or established patients*	N=43 40.9±17.3 72.1 11.8 11.8 2.9 5.9 25.7 Not reported Established	N=430 42.2±19.1, p=0.68 68.8, p=0.66 14.0, p=062 10.2, p=0.77 2.5, p=0.87 8.5, p=0.59 27.1, p=0.86 Not reported Established
Weinhandl 2012 (27)/ 2005-2008	Total number of patients (N) Mean age % male *Comorbidity (%)* Atherosclerotic heart disease Cerebrovascular disease Congestive heart failure Peripheral vascular disease Other cardiovascular disease Cancer Diabetes *Primary kidney disease (%)*	N=1873 52.2±14.8 64.2 24.0 8.3 26.9 20.9 20.0 9.1 40.6	N=9365 53.2±14.7, p=0.007* 62.3, p=0.46 22.7, p=0.33 8.1, p=0.79* 27.1, p=0.89* 20.05, p=0.75* 17.9, p=0.08* 7.3, p=0.01* 42.1, p=0.44*

	Diabetes Hypertension Glomerulonephritis or cystic kidney disease: *Incident or established patients*	27.3 19.3 30.3 Established	30.3 20.6 28.4 Established

*p-values calculated by us

Table V: *Patient characteristics at baseline for the studies assessed for HD home versus PD home*

Author year/ Study period	Patient characteristics at baseline	INTERVENTION HD home	CONTROL PD home
Kumar 2008 (20)/ 2003-07	Total number of patients (N) Age, median (range) % male *Comorbidity (%)* Diabetes *Primary kidney disease (%)* Diabetes Glomerulonephritis Hypertension Polycystic kidney *Incident or established patients*	N=22 52 (33-76) 73 41 41 32 9 4 Both	N=64 54 (21-82) 52, p=0.1 56, p=0.8 56 16 20 0 Both
Fong 2007 (15)/ 2006	Total number of patients (N) Mean age±SD % male *Comorbidity* Charlson index (mean±SD) *Primary kidney disease (%)* *Incident or established patients*	N=36 49±12 67 1.14±0.25 Not reported Established	N=57 61±13 55 1.18±0.33, p=0.14 Not reported Established

Table VI: *Patient characteristics at baseline for the studies assessed for APD home versus CAPD home*

Author year/ Study period	Patient characteristics at baseline	INTERVENTION APD	CONTROL CAPD
Bro 1999 (14)/ Not reported	Total number of patients (N) Mean age % male *Comorbidity (%)* Hypertension	N=17 50.2±4.6 47 41.1	N=17 54.2±4.2, p=ns 47, p=ns

	Iscemic heart disease Claudication Diabetes *Primary kidney disease (%)* Diabetes Hypertension Glomerulonephritis Interstitial nephritis Polycystic kidney disease: 5.9 *Incident or established patients*	11.8 5.9 0 23.5 5.9 17.6 5.9 5.9 Established	47.1, p=ns 5.9, p=ns 5.9, p=ns 5.9, p=ns 17,6, p=ns 5,9, p=ns 29.4, p=ns 0, p=ns 0, p=ns Established
Sanchez 2008 (24)/ 2003-2005	Total number of patients (N) Median age (range) % male *Comorbidity (%)* Diabetes *Primary kidney disease (%)* *Incident or established patients*	 N=98 59 (25-92) 54 70 Not reported Incident	 N=139 62 (18-89), p=0.031 47, p=ns 77, p=ns *Primary kidney disease (%)* Not reported Incident

Appendix 5- Description of transformation of the results to log relative risk and standard error

Comparison/ Outcome/ Author year	Data used in our meta-analyses logRR (SE)*	Data as presented in the articles	Description of the calculation
PDhome vs HDhospital/ Mortality			logRR: ln(1/RR) SE(logRR): $(\ln(1/CI_{low})-\ln(1/CI_{high}))/(2*1{,}96)$
Korevaar 2003	-1.2809 (0.7545)	HR HDhospital vs PD:3.6 (0.8-15.4) (adjusted, ITT)	
Andrikos 2008	-0.9076 (0.3675)	Reported mortality events/total: PD:8/48; HD:19/46	Standard 2x2-table
Ganeshadeva 2009	1.1725 (0.5581)	Kaplan-Meier survival: PD:82.45 %; HD: 94.52 % (ITT, do not tell if adjusted or not)	Standard 2x2-table
Jager 2001	0.1398 (0.2547)	RR mortality for PD: 1.15 (0.70-1.90) (ITT?, adjusted)	logRR: ln(RR) SE(logRR): $(\ln(CI_{high})-\ln(CI_{low}))/(2*1{,}96)$
Lee 2008	-0.0995 (0.2388)	% survival: PD: 87.9 % of 190 patients; HD: 86.6 % of 344 patients (ITT, do not tell if adjusted or not)	Standard 2x2-table (Assume 23 deaths for PD (12.1%) and 46 for HD (13.4%))
Vigneau 2000	2.3979 (1.4313)	Reported mortality events/total: PD: 5/14; HD: 0/14 (ITT, do not tell if adjusted or not)	Standard 2x2-table Because one cell in the 2x2-table is empty, all 4 cells are added with 0.5
Hospital days per patient per year			
Andrikos 2008	0.0652 (0.0456)	Days (median)/ patient/year: PD:5,23; HD:4.9	LogRR: Ln(PD/HD)

		(ITT, do not tell if adjusted or not)	SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Ganeshadeva 2009	0.19 (0.05)	Days/patient-months at risk: PD: 1.19; HD:0.98 (ITT, do not tell if adjusted or not)	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Verdalles 2010	-1.083 (3.5197)	Days (mean ±SD)/year: PD: 4.3 ±9.9; HD: 12.7±21.1 (ITT, do not tell if adjusted or not)	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(SD_{PD}^2/n_{PD}+SD_{HD}^2/n_{HD}
Vigneau 2000	1.6546 (6.1675)	Days (mean ±SD) during the 14 months risk period: PD: 34.0±19.0; HD:6.5±5.5 (ITT, do not tell if adjusted or not)	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(SD_{PD}^2/n_{PD}+SD_{HD}^2/n_{HD}
Hospital admissions per patient per year			
Andrikos 2008	0.13 (0.1)	Admissions per patient per year: PD: 1.14; HD:1 (ITT, do not tell if adjusted or not)	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Ganeshadeva 2009	0.3 (0.15)	Admissions per patient-month at risk: PD: 1 admission in 6 patient-months at risk; HD: 1 admission in 8.1 patient-months at risk. (ITT, do not tell if adjusted or not)	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Verdalles 2010	-0.87 (0.21)	Admissions per patient per year: PD: 0.36±0.63; HD:0.86±1	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(SD_{PD}^2/n_{PD}+SD_{HD}^2/n_{HD}
Cardiovascular events including			

arrhytmias			
Ganeshadeva 2009	-1.7917 (0.4151)	Mean events per patient- months at risk: PD: 1 in 278.5; HD: 1 in 68.4	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
All acute coronary syndromes			
Ganeshadeva 2009	-3.4188 (1.4298)	Mean events per patient- months at risk: PD: 0; HD: 1 in 177.6	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD}) Cells are added with 0.5
Cerebrovascular accidents (infarct and hemorrhages)			
Ganeshadeva 2009	-0.2267 (0.8047)	Mean events per patient- months at risk: PD: 1 in 756.0; HD: 1 in 888.0	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Dialysis modality access dysfunction			
Ganeshadeva 2009	-0.045 (0.19)	Mean events per patient- months at risk: PD: 1 in 39.4; HD: 1 in 55.5	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Dialysis modality related infections			
Ganeshadeva 2009	4.9226 (1.4218)	Mean events per patient- months at risk: PD: 1 in 38.6; HD: 1 in 125	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Pneumonia			
Ganeshadeva 2009	0.7701 (0.4373)	Mean events per patient- months at risk: PD: 1 in 139.5; HD: 1 in 444.0	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Septic arthritis			

Ganeshadeva 2009	0.1788 (0.5037)	Mean events per patient- months at risk: PD: 1 in 252.0; HD: 1 in 444.0	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
HDhome vs HD satellite/ Mortality			
Johansen 2009 NHD	-1.0217 (0.2602)	HR from Cox regression (NHD compared with CHD):0.36 (0.22-0.61) (ITT, do not tell if adjusted or not)	logRR: ln(RR) SE(logRR): (ln(CI_{high})- ln(CI_{low}))/(2*1,96)
Johansen 2009 SDHD	-0.4463 (0.3677)	HR from Cox regression (SDHD compared with CHD):0.64 (0.31-1.31) (ITT, do not tell if adjusted or not)	logRR: ln(RR) SE(logRR): (ln(CI_{high})- ln(CI_{low}))/(2*1,96)
Weinhandl 2012	-0.1393 (0.0556)	HR from Cox regression (DHHD vs satelitte): 0.87 (95% C.I.)(0.78-0.97) (ITT, do not tell if adjusted or not)	logRR: ln(RR) SE(logRR): (ln(CI_{high})- ln(CI_{low}))/(2*1,96)
Vascular access hospitalization			
Johansen 2009 NHD	0.27 (0.2)	HR from Cox regression (NHD compared with CHD): 1.31(0.88-1.94)	logRR: ln(RR) SE(logRR): (ln(CI_{high})- ln(CI_{low}))/(2*1,96)
Johansen 2009 SDHD	-0.34 (0.42)	HR from Cox regression (SDHD compared with CHD): 0.71 (0.31-1.64)	logRR: ln(RR) SE(logRR): (ln(CI_{high})- ln(CI_{low}))/(2*1,96)
Congestive heart			

failure hospitalization			
Johansen 2009 NHD	-0.14 (0.37)	HR from Cox regression regression (NHD compared with CHD):0.87 (0.42-1.81)	logRR: ln(RR) SE(logRR): $(\ln(CI_{high})- \ln(CI_{low}))/(2*1,96)$
Johansen 2009 SDHD	-0.26 (0.61)	HR from Cox regression regression (SDHD compared with CHD): 0.77 (0.23-2.53)	logRR: ln(RR) SE(logRR): $(\ln(CI_{high})- \ln(CI_{low}))/(2*1,96)$
PDhome vs HDsatellite/ Infected-related hospitalization			
Aslam 2006	0.5481 (0.265)	HR from Cox regression (PDhome vs HDsatelitte): 1.73 (95% C.I.: 1.03-2.91)	logRR: ln(RR) SE(logRR): $(\ln(CI_{high})- \ln(CI_{low}))/(2*1,96)$
Williams 2011	0.131 (0.3436)	HR from Cox regression (PDhome vs HDsatelitte): 1.14 (95% C.I.: 0.58-2.23)	logRR: ln(RR) SE(logRR): $(\ln(CI_{high})- \ln(CI_{low}))/(2*1,96)$
Pneumonia-related hospitalizations			
Aslam 2006	-1.2528 (0.8516)	Admissions/year: PD: 0.02 HD: 0.07	LogRR: Ln(PD/HD) SE(ln(RR)): $Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})$
Williams 2011	0.2513 (2.1353)	Admissions/1000 treatment days PD:0.09 HD: 0.07	LogRR: Ln(PD/HD) SE(ln(RR)): $Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})$

Bacteremia-related hospitalization			
Aslam 2006	-2.7685 (1.4334)	Admissions/year: PD: 0 HD: 0.10	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD}) Cells are added with 0.5
Williams 2011	-1.7918 (2.5427)	Admissions/1000 treatment days PD: 0.03 HD: 0.18	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Peritonitis-related hospitalization			
Aslam 2006	4.2504 (1.4372)	Admissions/year: PD: 0.19 HD: 0	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})
Williams 2011	1.2321 (1.8537)	Admissions/1000 treatment days: PD: 0.24 HD:0.07	LogRR: Ln(PD/HD) SE(ln(RR)): Sqrt(1/(PD*n_{PD})+1/(HD*n_{HD})

*log (Risk Ratio) Standard error

Appendix 6- Grade Evidence Tables

PD vs HD hospital

Quality assessment							Summary of findings					
							No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	pd	hdhospital	Relative (95% CI)	Absolute		
Mortality (follow-up 5 years; from randomization to death or censoring.)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2,3,4]	none	5/20 (25%)	9/18 (50%)	RR 0.28 (0.06 to 1.22)	360 fewer per 1000 (from 470 fewer to 110 more)	⊕⊕OO LOW	CRITICAL
								25%		180 fewer per 1000 (from 235 fewer to 55 more)		
Mortality - Observational (follow-up 4-60 months)												
5[5]	observational studies	no serious limitations	serious[6]	no serious indirectness	serious[3,4]	none	47/315 (14.9%)	69/478 (14.4%)[7]	RR 1.11 (0.59 to 2.1)	16 more per 1000 (from 59 fewer to 159	⊕OOO VERY LOW	CRITICAL

										more)		
Mortality short term - Observational (follow-up 12-14 months)												
3	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[3,4]	none	39/267 (14.6%)	50/432 (11.6%)	RR 2.08 (0.6 to 7.28)	125 more per 1000 (from 46 fewer to 727 more)	⊕OOO VERY LOW	IMPORTANT
Mortality long term-Observational (follow-up median 28-48.5 months; Andrikos; Jager)												
2	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[3,4]	none	8/48 (16.7%)	19/46 (41.3%)[8]	RR 0.70 (0.25 to 1.96)	124 fewer per 1000 (from 310 fewer to 397 more)	⊕OOO VERY LOW	IMPORTANT
Hospital days admitted per year (follow-up 6-60 months)												
4	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	no serious impreci-sion	none	0/100 (0%)[9]	5% 12%	RR 1.13 (1.04 to 1.23)	6 more per 1000 (from 2 more to 12 more) 16 more per 1000 (from 5 more to 28 more)	⊕⊕OO LOW	CRITICAL
Hospital admissions (per patient per year) (follow-up 6-60 months)												
3	observa-tional studies	no serious limita-tions	serious[6]	no serious indirect-ness	serious[4]	none	0/0 (0%)	0/0 (0%)	RR 0.89 (0.5 to	0 fewer per 1000	⊕OOO VERY LOW	CRITICAL

									1.55)	(from 0 fewer to 0 more)		
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Quality of life - RCT QALY score adjusted (follow-up 2 years; Better indicated by lower values)												
1	random-ised trials	serious[1]	no serious inconsisten-cy	no serious indirect-ness	serious[2,10]	none	0	0	-	MD 0.05 lower (0.15 lower to 0.05 higher)	⊕⊕OO LOW	IMPORTANT
Quality of life - Observational SF-36 Physical (Better indicated by lower values)												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,10]	none	0	0	-	MD 1.10 higher (3.15 lower to 5.35 higher)	⊕OOO VERY LOW	IMPORTANT
Quality of life - Observational SF-36 mental (Better indicated by lower values)												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,10]	none	0	0	-	MD 2.60 lower (10.69 lower to 5.49 higher)	⊕OOO VERY LOW	IMPORTANT
Infections (follow-up mean 14 months; (Vigneau))												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,3,4]	none	9/14 (64.3 %)	4/14 (28.6%)	RR 2.25 (0.9 to 5.62)	357 more per 1000 (from 29	⊕OOO VERY LOW	IMPORTANT

										fewer to 1320 more)		
Cardiovascular events including arrhytmias (follow-up 1 years; (Ganeshadeva))												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,3]	none	0/0 (0%)	0/0 (0%)[11] 0%	RR 0.17 (0.07 to 0.38)	0 fewer per 1000 (from 0 fewer to 0 few-er) 0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	IMPORTANT
All acute coronary syndromes (follow-up 1 years; Ganeshadeva)												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,3]	none	0/0 (0%)	0/0 (0%)[12] 0%	RR 0.03 (0 to 0.54)	0 fewer per 1000 (from 0 fewer to 0 few-er) 0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	IMPORTANT
Cerebrovascular accidents (infarct and hemorrhages) (follow-up 1 years; (Ganeshadeva))												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,3,4]	none	0/0 (0%)	0/0 (0%)[13] 0%	RR 0.8 (0.16 to 3.86)	0 fewer per 1000 (from 0 fewer to 0 more) 0 fewer per 1000 (from 0	⊕OOO VERY LOW	IMPORTANT

										fewer to 0 more)		
Dialysis modality access dysfunctions (follow-up 1 years; Ganeshadeva)												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,3,4]	none	0/0 (0%)	0/0 (0%)[14] 0%	RR 0.96 (0.66 to 1.39)	0 fewer per 1000 (from 0 fewer to 0 more) 0 fewer per 1000 (from 0 fewer to 0 more)	⊕OOO VERY LOW	IMPORTANT
Dialysis modality related infections (follow-up 1 years; Ganeshadeva)												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,3]	none	0/0 (0%)	0/0 (0%)[15] 0%	RR 137.36 (8.46 to 2228.93)	0 more per 1000 (from 0 more to 0 more) 0 more per 1000 (from 0 more to 0 more)	⊕OOO VERY LOW	IMPORTANT
Pneumonia (follow-up 1 years; Ganeshadeva)												
1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,3,4]	none	0/0 (0%)	0/0 (0%)[16] 0%	RR 2.16 (0.92 to 5.09)	0 more per 1000 (from 0 fewer to 0 more) 0 more per 1000 (from 0 fewer to 0 more)	⊕OOO VERY LOW	IMPORTANT
Septic Arthritis (follow-up 1 years; Ganeshadeva)												

1	observa-tional studies	no serious limita-tions	no serious inconsisten-cy	no serious indirect-ness	serious[2,3,4]	none	0/0 (0%)	0/0 (0%)[17]	RR 1.2 (0.45 to 3.21)	0 more per 1000 (from 0 fewer to 0 more)	⊕OOO VERY LOW	IMPORTANT
								0%		0 more per 1000 (from 0 fewer to 0 more)		

[1] The study was planned/powered to 100 patients. Study stopped after 38 patients due to inclusion problems.

[2] Only one study. Unclear reproducibility

[3] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>)

[4] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "apprecia-ble benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

[5] One more study reported mortality, but only as no sigificant difference.

[6] Unexplained heterogeneity

[7] Events taken from 4 of the 5 studies (Andrikos, Ganeshadeva, Lee, Vigneau)

[8] Event numbers only available from Adrikos (Jager had no numbers).

[9] Have no events numbers

[10] add text for impreci for contionous variable MD??

[11] Background risk of CV events in HD patients in hospital is 1 per 68,4 patient month at risk

[12] Bacground risk of all acute coranary syndromes in HD patients in hospital is 1 per 177,6 patient month at risk

[13] Bacground risk of cerebrovascular accidents in HD patients in hospital is 1 per 880,0 patient month at risk

[14] Bacground risk of dialysis modality access dysfuntion in HD patients in hospital is 1 per 55,5 patient month at risk

[15] Bacground risk of dialysis modality related infections in HD patients in hospital is 1 per 125 patient month at risk

[16] Background risk of pneumonia in HD patients in hospital is 1 per 444 patient month at risk

[17] Background risk of septic arthritis in HD patients in hospital is 1 per 444 patient month at risk

HD satelitte vs HD hospital

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	hd satelitte	hd hospital	Relative (95% CI)	Absolute		
Patients hospitalised (follow-up 1 years; Roderick)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	None	141/394 (35.8%)	153/342 (44.7%)	RR 0.8 (0.67 to 0.95)	89 fewer per 1000 (from 22 fewer to 148 fewer)	⊕OOO VERY LOW	IMPORTANT
Access related hospitalisation (follow-up 1 years; Roderick)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2,3]	None	62/394 (15.7%)	61/342 (17.8%)	RR 0.88 (0.64 to 1.22)	21 fewer per 1000 (from 64 fewer to 39 more)	⊕OOO VERY LOW	IMPORTANT
Access formation hospitalisation (follow-up 1 years; Roderick)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2,3]	None	40/394 (10.2%)	42/342 (12.3%)	RR 0.83 (0.55 to 1.24)	21 fewer per 1000 (from 55 fewer to 29 more)	⊕OOO VERY LOW	IMPORTANT
Cardiac or vascular hospitalisation (follow-up 1 years; Roderick)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2,3]	None	14/394 (3.6%)	23/342 (6.7%)	RR 0.53 (0.28 to 1.01)	32 fewer per 1000 (from 48 fewer to 1 more)	⊕OOO VERY LOW	IMPORTANT
Infections (not access related) hospitalisation (follow-up 1 years; Roderick)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2]	None	19/394 (4.8%	30/342 (8.8%	RR 0.55 (0.32	39 fewer per 1000 (from 4	⊕OOO VERY LOW	IMPORTANT

						)	)	to 0.96)	fewer to 60 fewer)		
Length of stay in hospital (days/per patient) (follow-up mean 1 years; Better indicated by lower values)											
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,3]	None	394	342	-	MD 1.10 lower (2.6 lower to 0.4 higher)	⊕OOO VERY LOW	IMPORTANT
Quality of life - EQ-5D utilities off dialysis (measured with: EQ VAS scores; Better indicated by lower values)											
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	0	0	-	MD 0.00 higher (0.05 lower to 0.05 higher)	⊕OOO VERY LOW	IMPORTANT
Quality of life - SF-36 physical score (Better indicated by lower values)											
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	0	0	-	MD 0.02 higher (2.11 lower to 2.15 higher)	⊕OOO VERY LOW	IMPORTANT
Quality of life - SF-36 mental score (Better indicated by lower values)											
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	0	0	-	MD 4.39 lower (6.58 to 2.2 lower)	⊕OOO VERY LOW	IMPORTANT
Quality of life - KDQOL (Better indicated by lower values)											
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	0	0	-	MD 7.5 higher (1.33 to 13.67 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Only one study. Unclear reproducibility

[2] Total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881 <http://www.annals.org/cgi/content/abstract/146/12/878>)

[3] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

HD home vs HD satelitte

Quality assessment							Summary of findings					
							No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	hd home	hd satelitte	Relative (95% CI)	Absolute		
Mortaltiy (follow-up 21-86 months; Johansen (2 comparisions) and Weinhandl)												
3	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious	none	275/2010 (13.7%)[2]	420/10735 (3.9%)[1]	RR 0.60 (0.33 to 1.1)	16 fewer per 1000 (from 26 fewer to 4 more)	⊕⊕OO LOW	CRITICAL
Vascular access hospitalisation (follow-up 53-86 months; Johansen (2 comparisions in one study))												
2	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	Serious[2]	none	0/0 (0%)	0/0 (0%) 0%	RR 1.08 (0.62 to 1.88)	0 more per 1000 (from 0 fewer to 0 more) 0 more per 1000 (from 0 fewer to 0 more)	⊕OOO VERY LOW	IMPORTANT
Congestive heart failure hospitalisation (follow-up 53-86 months; Johansen (2 comparisions in one study))												
2	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	Serious[2]	none	0/0 (0%)	0/0 (0%)	RR 0.84 (0.45 to	0 fewer per 1000 (from 0	⊕OOO VERY LOW	IMPORTANT

									1.56)	fewer to 0 more)		
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		

[1] Events measured as deaths /1000 patient-years

[2] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

PD versus HD satelitte

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	pd	hd satelitte	Relative (95% CI)	Absolute		
Mortality (follow-up 15-18 months; Aslam)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2]	none	7/62 (11.3 %)	33/119 (27.7 %)	RR 0.41 (0.19 to 0.87)	164 fewer per 1000 (from 36 fewer to 225 fewer)	⊕OOO VERY LOW	CRITICAL
Infection related hospitalisations (follow-up 15-27.5 months; Aslam ; Williams)												
2	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,3]	none	18/71 (25.4 %)	17/97 (17.5%)[4]	RR 1.48 (0.98 to	84 more per 1000	⊕OOO VERY LOW	IMPORTANT

									2.23)	(from 4 fewer to 216 more)		
								0%		0 more per 1000 (from 0 fewer to 0 more)		
Complications - Pneumonia (follow-up 15-27.5 months; Aslam; Williams)												
2	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,3]	none	0/0 (0%)	0/0 (0%)	RR 0.35 (0.07 to 1.66)	0 fewer per 1000 (from 0 fewer to 0 more)	⊕OOO VERY LOW	IMPORTANT
								0%		0 fewer per 1000 (from 0 fewer to 0 more)		
Complications - Bacteremia (follow-up 15-27.5 months; Aslam, Williams)												
2	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	0/0 (0%)	0/0 (0%)	RR 0.08 (0.01 to 0.92)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	IMPORTANT
								0%		0 fewer per 1000 (from 0 fewer		

										to 0 fewer)		
Complications - Peritonitis (follow-up 15-27.5 months; Aslam, Williams)												
2	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	None	0/0 (0%)	0/0 (0%) 0%	RR 19.46 (1.05 to 362.32)	0 more per 1000 (from 0 more to 0 more) 0 more per 1000 (from 0 more to 0 more)	⊕OOO VERY LOW	IMPORTANT

[1] Total number of events less than 300

[2] Only one study. Unclear reproducibility

[3] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

[4] Events only from one of the studies (Williams)

HD home vsPD

Quality assessment							**Summary of findings**					**Importance**
							No of patients		**Effect**		**Quality**	
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**hd home**	**pd**	**Relative (95% CI)**	**Absolute**		
Complications- Patients admitted diagnosed with Cardiac (angina, myocardial infarction, atrial fibrillation (follow-up 20-22 months; Kumar)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2,3]	none	4/22 (18.2%)	8/64 (12.5%)	RR 1.45 (0.49	56 more per	⊕OOO VERY	IMPORTANT

									to 4.36)	1000 (from 64 fewer to 420 more)	LOW	
Complications -Hospital days/patients for those diagnosed with Cardiac (angina, myocardial infarction, atrial fibrillation) (follow-up 20-22 months; Kumar)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[2,3]	none	20/22 (90.9 %)	41/64 (64.1 %)	RR 1.42 (1.13 to 1.78)	269 more per 1000 (from 83 more to 500 more)	⊕OOO VERY LOW	IMPORTANT
Complications - Patients admitted diagnosed with infectious (sepsis, cellulitis, abscess, urinary tract infection, pneumonia, gangrene) (follow-up 20-22 months; Kumar)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2,3]	none	1/22 (4.5%)	12/64 (18.8 %)	RR 0.24 (0.03 to 1.76)	142 fewer per 1000 (from 182 fewer to 142 more)	⊕OOO VERY LOW	IMPORTANT
Complications- Hospital days/patients for those diagnosed with infectious (sepsis, cellulitis, abscess, urinary tract infection, pneumonia, gangrene) (follow-up 20-22 months; Kumar)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[2,3]	none	6/22 (27.3 %)	125/64 (195.3 %)	RR 0 (0 to 0)[4]	1953 fewer per 1000 (from 1953 fewer to 1953 fewer)	⊕OOO VERY LOW	IMPORTANT

								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)		
Complications- Patients admitted diagnosed with ESRD related congestive heart failure (follow-up 20-22 months; Kumar)												
1	observa-tional studies	no seri-ous limi-tations	no serious incon-sistency	no serious indirect-ness	seri-ous[1,2,3]	none	1/22 (4.5%)	4/64 (6.3%)	RR 0.73 (0.09 to 6.16)	17 fewer per 1000 (from 57 fewer to 322 more)	⊕OOO VERY LOW	IM-PORTANT
Complications-Hospital days/ for thos diagnosed with ESRD related Congestive failure (follow-up 20-22 months; Kumar)												
1	observa-tional studies	no seri-ous limi-tations	no serious incon-sistency	no serious indirect-ness	serious[1,2]	none	2/22 (9.1%)	17/64 (26.6%)	RR 0.34 (0.09 to 1.36)	175 fewer per 1000 (from 242 fewer to 96 more)	⊕OOO VERY LOW	IM-PORTANT
Complicatio-Patients admitted diagnosed with ESRD related Arteriovenous access complication (access infection, clotting, bleeding, endocarditis) (follow-up 20-22 months; Kumar)												
1	observa-tional studies	no seri-ous limi-tations	no serious incon-sistency	no serious indirect-ness	serious[2]	none	5/22 (22.7%)	1/64 (1.6%)	RR 14.55 (1.8 to 117.8)	212 more per 1000 (from 12 more to 1825	⊕OOO VERY LOW	IM-PORTANT

										more)		
Complications-Hospital days/patients for those diagnosed with ESRD related Arteriovenous access complications (access infection, clotting, bleeding, endocarditis) (follow-up 20-22 months; Kumar)												
1	observa-tional studies	no seri-ous limi-tations	no serious incon-sistency	no serious indirect-ness	serious[2]	none	53/22 (240.9%)	1/64 (1.6%)	RR 0 (0 to 0)[4]	16 fewer per 1000 (from 16 fewer to 16 fewer)	⊕OOO VERY LOW	IM-PORTANT
Complications-Patients admitted diagnosed with peritonitis or tunnel infections (follow-up 20-22 months; Kumar)												
1	observa-tional studies	no seri-ous limi-tations	no serious incon-sistency	no serious indirect-ness	serious[2]	none	0/22 (0%)	19/64 (29.7%)	RR 0.07 (0 to 1.15)	276 fewer per 1000 (from 297 fewer to 45 more)	⊕OOO VERY LOW	IM-PORTANT
Complications-Hospital days/patients for those diagnosed with peritonitis or tunnel infections (follow-up 20-22 months; Kumar)												
1	observa-tional studies	no seri-ous limi-tations	no serious incon-sistency	no serious indirect-ness	serious[2]	none	0/22 (0%)	138/64 (215.6%)	RR 0 (0 to 0)[4]	2156 fewer per 1000 (from 2156 fewer to 2156 fewer)	⊕OOO VERY LOW	IM-PORTANT
Quality of life- KDCS (Better indicated by lower values)												
1	observa-tional studies	no seri-ous limi-tations	no serious incon-sistency	no serious indirect-ness	serious[2,3]	none	0	0	-	MD 6.90 higher (2.8	⊕OOO VERY LOW	IM-PORTANT

										lower to 16.6 higher)		
Physcical component summary (Better indicated by lower values)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[2,3]	none	0	0	-	MD 2.70 higher (3.02 lower to 8.42 higher)	⊕OOO VERY LOW	IMPORTANT
Mental component summary (Better indicated by lower values)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[2,3]	none	0	0	-	MD 1.60 higher (9.88 lower to 13.08 higher)	⊕OOO VERY LOW	IMPORTANT

[1] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

[2] Total number of events less than 300

[3] Only one study. Unclear reproducibility

[4] Not estimable

APD vs CAPD

Quality assessment							Summary of findings					Im-portance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	APD		Relative (95% CI)	Absolute	Quality	
Mortality - mortality 1 year (follow-up 1 years; Sanchez)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2]	none	18/98 (18.4%)	53/139 (38.1%)	RR 0.48 (0.3 to 0.77)	198 fewer per 1000 (from 88 fewer to 267 fewer)	⊕OOO VERY LOW	CRITICAL
Mortality - mortality 2 years (follow-up 2 years; Sanchez)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2]	none[1,2]	37/98 (37.8%)	71/139 (51.1%)	RR 0.74 (0.55 to 1)	133 fewer per 1000 (from 230 fewer to 0 more)	⊕OOO VERY LOW	CRITICAL
Mortality - mortality 3 years (follow-up 3 years; Sanchez)												
1	observational studies	no serious limitations	no serious inconsistency	no serious indirectness	serious[1,2]	none	43/98 (43.9%)	81/139 (58.3%)	RR 0.75 (0.58 to 0.98)	146 fewer per 1000 (from 12 fewer to 245 fewer)	⊕OOO VERY LOW	CRITICAL

RCT peritonitis (follow-up 6 months)												
1	random-ised tri-als	serious[3]	no serious incon-sistency	no serious indirect-ness	serious[1,2,4]	none	1/17 (5.9 %)	2/17 (11.8 %)	RR 0.50 (0.05 to 5.01)	59 fewer per 1000 (from 112 fewer to 472 more)	⊕⊕OO LOW	CRITI-CAL
RCT- Exit-Site Infection (follow-up 6 months; Bro)												
1	random-ised tri-als	serious[3]	no serious incon-sistency	no serious indirect-ness	serious[1,2,4]	none	1/17 (5.9 %)	1/17 (5.9 %)	RR 1.00 (0.07 to 14.72)	0 few-er per 1000 (from 55 fewer to 807 more)	⊕⊕OO LOW	IM-PORTAN T
RCT Tunnel Infection (follow-up 6 months)												
1	random-ised tri-als	serious[3]	no serious incon-sistency	no serious indirect-ness	serious[1,2,4]	none	1/17 (5.9 %)	0/17 (0%)	RR 3.00 (0.13 to 68.84)	0 more per 1000 (from 0 few-er to 0 more)	⊕⊕OO LOW	IM-PORTAN T
Observational study-peritonitis (follow-up 0-3 years; Sanchez)												
1	observa-tional studies	no seri-ous limi-tations	no serious incon-sistency	no serious indirect-ness	serious[1,2]	none	0/0 (0%)	0/0 (0%)	Not esti-mable	0 few-er per 1000 (from 0 few-er to 0 fewer)	⊕OOO VERY LOW	IM-PORTAN T
RCT QoL (follow-up 6 months; Better indicated by lower values)												
1	random-ised tri-als	serious[3]	no serious incon-sistency	no serious indirect-ness	very seri-ous[2,4]	none	0	0	-	MD 0 higher (0 to 0	⊕OOO VERY	IM-PORTAN T

										high-er)[5]	LOW	

[1] Total number of events less than 300

[2] Only one study. Unclear reproducibility

[3] High drop-outs. In APD 4 of original 17, in CAPD 5 of original 17

[4] 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.

[5] Reported as no difference

Appendix 7- Forest plots not shown under Results

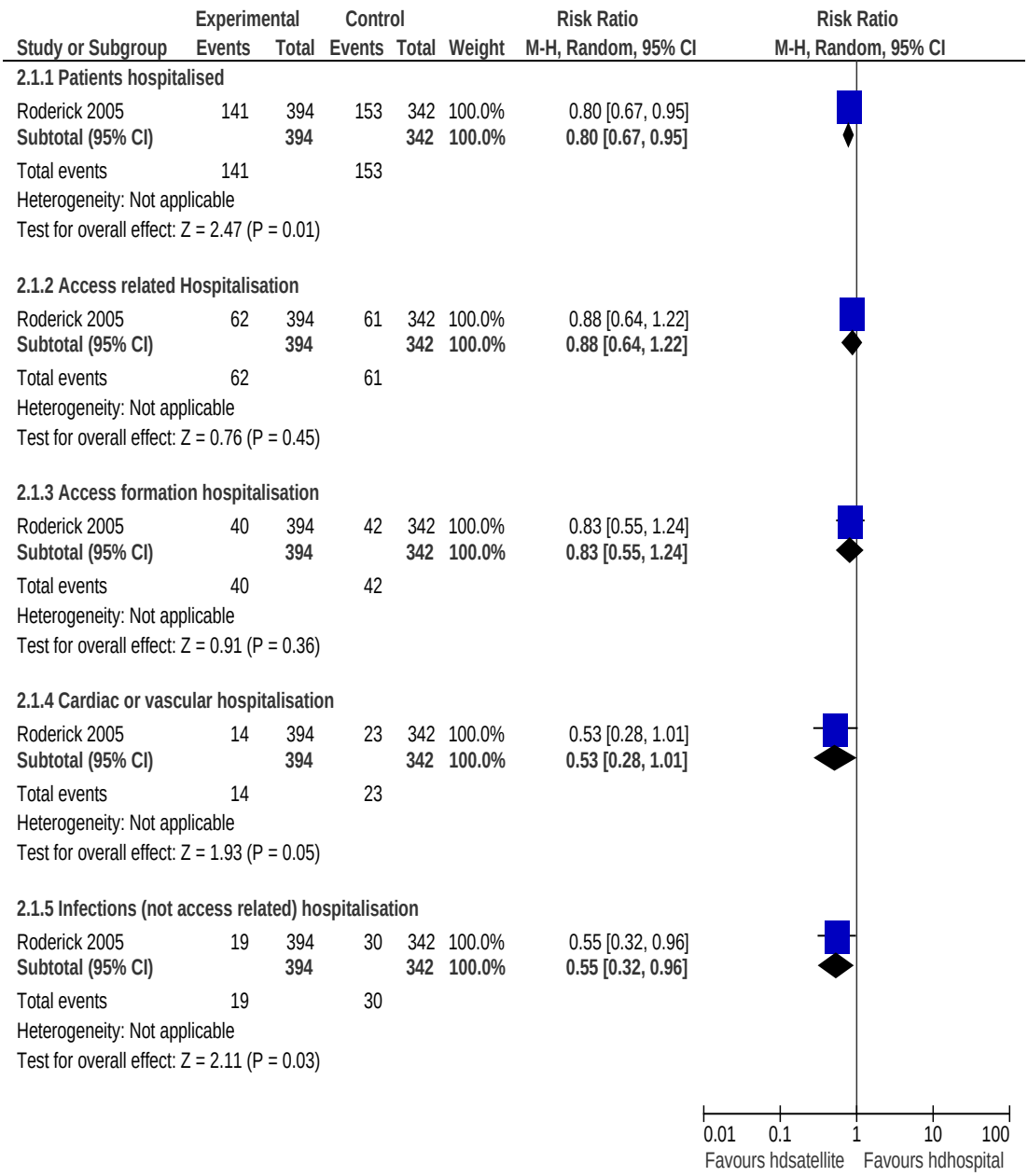


Figure I *Analyses of complications for the comparison HD satellite versus HD hospital*

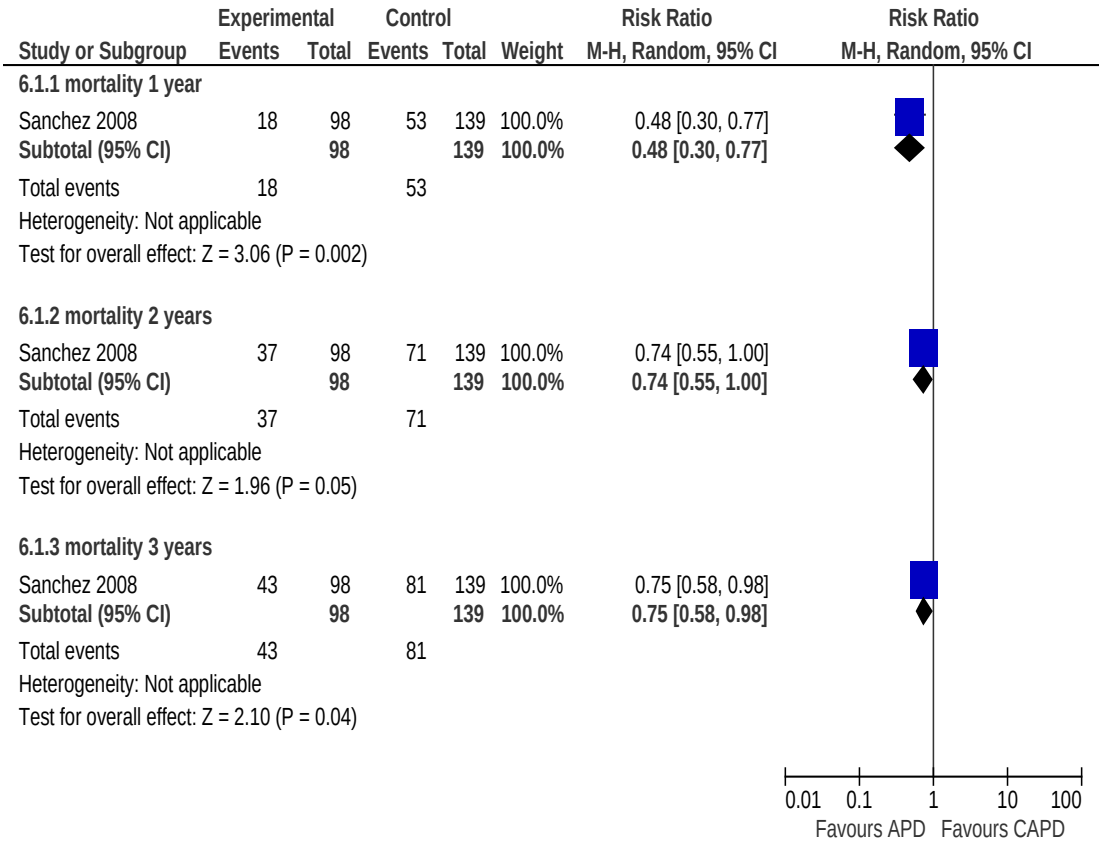


Figure II *Analyses of mortality at 1, 2 and 3 years for the comparison APD versus CAPD*

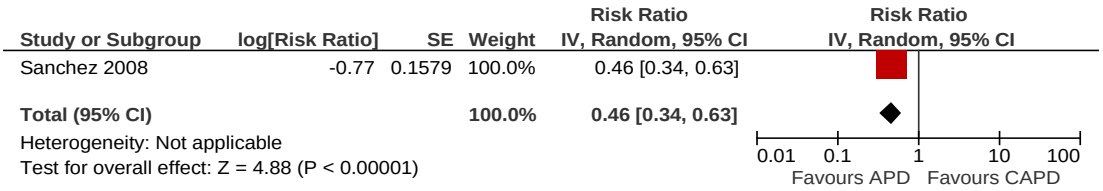


Figure III *Analyses of the documentation for peritonitis from the observational study for the comparison APD versus CAPD*

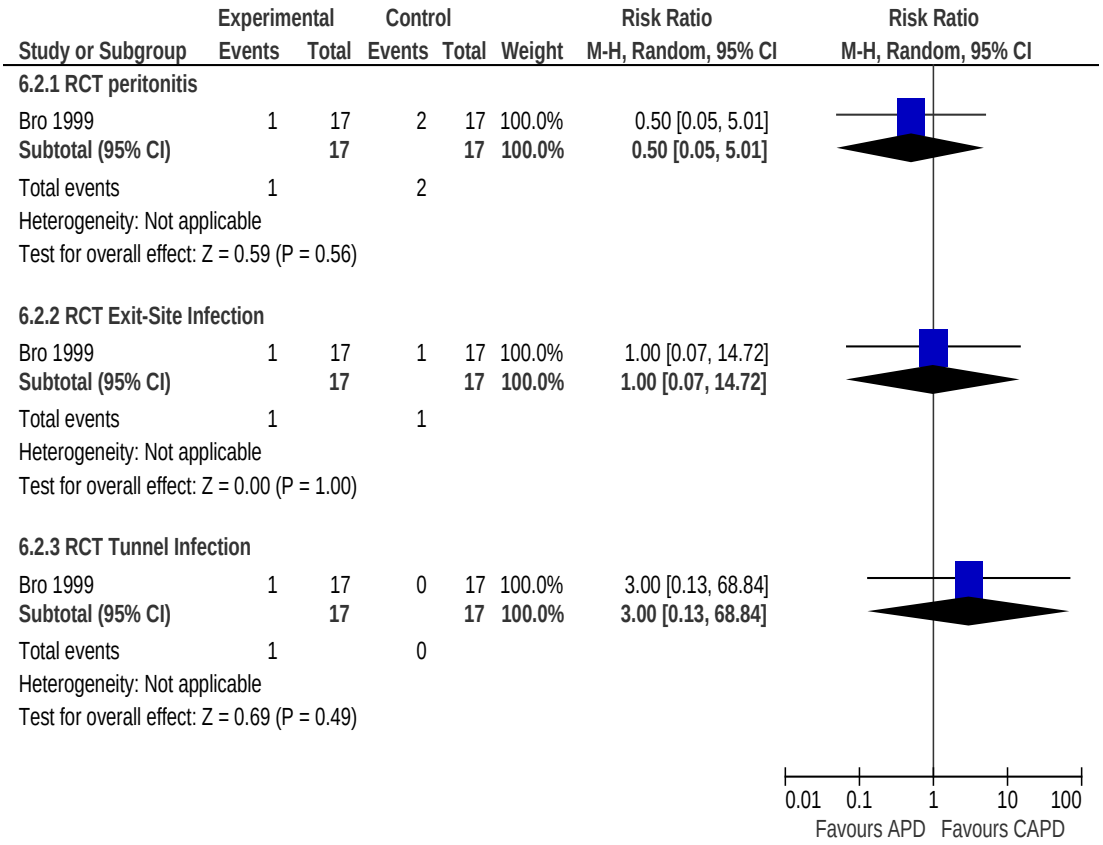
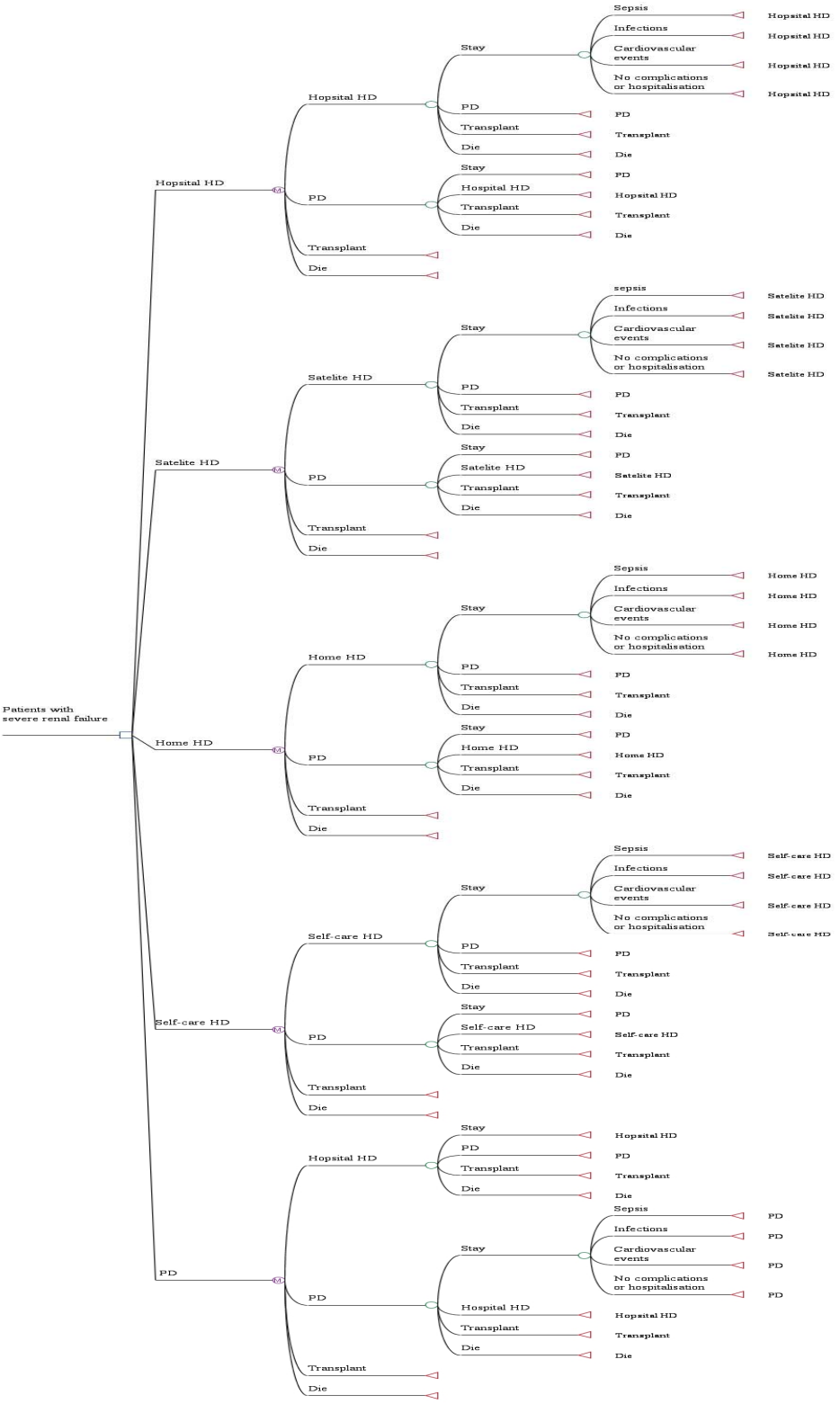


Figure IV *Analyses of complications from the RCT for the comparison APD versus CAPD*

Appendix 8- Model structure



Appendix 9- Costs

Table I. *Staff costs*

	Physician	Nurse	Other personnel [a]
Mean salary per month [b]	71,800 [c]	37,600	40,700
Average monthly working time in hours [d]	181	138	120,4
Mean cost per hour (incl. social expenses (x1.4)	557	383	473

[a] Incl. Secretary, medical technician, nutritionist, psychiatrist, physiotherapist, surgeon, operation room nurse
[b] Ref. http://www.ssb.no/lonnhelse
The mean salary per month for personnel was multiplied by 1,4 to account for social expenses. Not including overtime and extra shifts.
[c] Including payments to physicians for on-call services/UTA (utvidet tjeneste/arbeidstid)
[d] Ref. http://www.ssb.no/arbeid-og-lonn/artikler-og-publikasjoner/stort-omfang-av-deltidsarbeid

Table II. *Standard packages for blood test for dialysis patients* *

a: Hemodialysis

	HD
Monthly blood test	Hemoglobin, hematocrit, urea, reticulocyte hemoglobin, WBC, platelets, ferritin, iron, TIBC, venous acid base, sodium, potassium, calcium, phosphate, creatinine, albumin, CRP
Monthly blood test after dialysis	Sodium, potassium, calcium, phosphate, urea creatinine, albumin
Additional tests every 3 months	SR, uric acid,urea, bilirubin, glucose, ASAT, ALAT, ALP, total protein, PTH, β2 microglobulin
Additional tests every 6 months	Cystatin c, total cholesterol, HDL/LDL cholesterol, triglycerides Hepatitis A,B,C and HIV serology, uric acid, urea

b: Peritoneal dialysis

	PD
Monthly blood test	Hemoglobin, reticulocytes, WBC, platelets, venous acid-base, glucose, sodium, potassium, calcium total and calcium adjusted for albumin, urea, creatinine, albumin, CRP, cystatin c
Additional tests every 3 months	Ferritin, iron, urea, Total iron binding capacity (TIBC), β2 microglobulin, parathyroid hormone (PTH), HbA1c (diabetics patients)
Additional tests every 6 months	SR, HbA1c (all patients), bilirubin, uric acid, ASAT, ALAT ATLP, total cholesterol, HDL-,LDL- cholesterol, triglycerides

*Ref. Oslo university hospital (personal communication by head of dialysis department dr. med Aud-E Stenehjem)

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