NICE advice

The NxStage System One NX1000-1 home haemodialysis device for renal replacement therapy in chronic kidney disease

Medtech innovation briefing
Published: 19 November 2014

www.nice.org.uk/guidance/mib12

Summary

The NxStage System One is a haemodialysis system for renal replacement therapy to be used at home or while travelling. The system can run from standard home electricity and water supplies, and is smaller than standard home haemodialysis systems.

Effectiveness	Adverse events and safety
• The available evidence comes from 7 published studies (reported in 9 publications) involving a total of 12,604 people. • Four small feasibility studies (n=4, 5, 25 and 78) confirmed at least equivalent safety and efficacy between standard in-centre and daily home haemodialysis with the NxStage System One. • Two multicentre cohort studies (n=291 and 11,228) showed an improvement in health-related quality of life and modest improvements in survival compared with standard in-centre haemodialysis 3 times per week. • A large single-centre retrospective cohort study (n=973) showed similar patient survival and better technique survival (the time between starting 1 type of RRT and switching to another) for daily home haemodialysis with the NxStage System One compared with peritoneal dialysis. • No studies were identified where the NxStage System One was compared with home haemodialysis using conventional equipment.	• A small single-centre case series study (n=3) reported dialyser-induced thrombocytopenia in 3 young people using the gamma sterilized PUREMA dialyser, which is part of the standard NxStage circuit. The adverse reaction was resolved in all 3 people when the dialyser and circuit were changed. • A feasibility study (n=25) reported the following adverse events in adults using the NxStage System One: blood under-heating, muscle cramping, hypotension, headache, dizziness and fatigue. The incidence of adverse events was higher when the system was used in-centre than when used in the home.

Cost and resource use	Technical factors
• Limited cost information is available for the NxStage System One. • The Manufacturer, NxStage Medical, is unable to provide information on the purchase cost of the NxStage System One. Instead, it presents the cost on a price-per-treatment basis that takes a number of variables into account. The manufacturer claims that the average price per treatment across all programmes is approximately 60% of the NHS tariff price for home haemodialysis.	• The NxStage System One is a transportable haemodialysis machine intended for use in the home. The NX1000-1 is currently the only model of this system available in the UK. • The device functions with a standard mains electrical and water supply, without the need for conversion of domestic power or water supplies. • A clean and safe area is required in the home to accommodate a 2-week supply of dialysis consumables.

Introduction

Chronic kidney disease (CKD) is the loss of kidney function. Symptoms may include tiredness, swollen hands and feet, shortness of breath, nausea and blood in urine. These symptoms usually do not present until CKD has reached an advanced stage, referred to as stage 5. The most common risk factors for developing CKD are hypertension (high blood pressure), diabetes and a family history of CKD (NHS Choices, 2012).

Kidney function is measured by estimating the glomerular filtration rate (GFR). This is a test to estimate how much waste fluid the kidneys can remove from blood in a minute. When a person's GFR is less than 15 mL/min/1.73 m^2, stage 5 CKD is diagnosed.

People diagnosed with stage 5 CKD often need renal replacement therapy (RRT) in order to sustain life. In 2012, 54,824 adults and 861 children and young people in the UK had RRT, with an incidence of 108 new people per 1 million population (Fogarty and Cullen, 2013).

A kidney transplant is considered the gold standard therapeutic option for people with

stage 5 CKD who need RRT. In 2012/13, 3000 kidney transplants were done in the UK. Transplanted kidney survival rates are reported to be 85–95% after 1 year, 70–80% after 5 years and 50–60% after 15 years (NHS Choices, 2013b). People with CKD who are waiting for a transplant or who do not meet the inclusion criteria for transplantation have dialysis, unless they elect for palliative care. Dialysis is the process of filtering the blood to remove any harmful waste products, extra salt and water. There are two forms of dialysis: haemodialysis and peritoneal dialysis (NHS Choices, 2013a).

Haemodialysis is the removal of metabolic waste products from the blood through a semi-permeable membrane. Blood is taken from the body through an arteriovenous fistula, intravenous catheter or synthetic graft (Fogarty and Cullen, 2013). The blood is passed into a dialysis machine which contains a semi-permeable membrane (NHS Choices, 2013a).The blood flows past a counter-flow of dialysate solution, and the waste products in the blood diffuse across the membrane into the solution. The dialysate solution contains ions such as sodium, calcium, potassium and magnesium, chloride and bicarbonate. The concentration of these ions is set specifically to meet each user's needs. People whose CKD is being treated with conventional haemodialysis may have to limit their fluid intake to 1.5 litres per day (less for children) and are subject to strict dietary controls to limit their intake of sodium, potassium and phosphorus (NHS Choices, 2013a).

Conventional haemodialysis can take place in a hospital, a satellite unit or at home. Each haemodialysis session lasts approximately 4 hours, and is repeated 3 times per week. NICE's technology appraisal guidance on home compared with hospital haemodialysis for patients with end-stage renal failure recommends that everyone who is suitable for home haemodialysis should be offered the choice. In 2012, 1080 people in the UK were using home haemodialysis (Fogarty and Cullen, 2013). People choosing home haemodialysis, and their caregivers, must take active responsibility for their treatment, but it has the potential to be clinically effective and provide an increase in quality of life for patients, family and caregivers (Hothi et al. 2013 and Young et al. 2012).

Peritoneal dialysis can also take place in either a health care setting or at home. In this treatment, metabolic waste products from the blood diffuse through the peritoneum (the semi-permeable membrane that surrounds the abdominal organs) rather than through a synthetic membrane outside of the body. The waste products diffuse into dialysis fluid, which is added into the abdominal cavity. The dialysis fluid is added and removed from the body through a catheter, which is surgically inserted into the person's abdomen and remains in place permanently (NHS Choices, 2013a).

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

CE marking

The NxStage System One first received a CE mark in April 2004. The current CE mark is held by NxStage Medical Inc. and has been valid since April 2014.

The individual components of the NxStage System One are listed below; all are CE marked as Class IIb medical devices other than the Express Fluid Warmer and the Fluid Warming System which are Class IIa:

- The cycler.
- Fluid warming devices:
  - Express Fluid Warmer.
  - The Fluid Warming System.

- The dialyser sets, made up of:
  - One of the following cartridges must be fitted to operate the system:
    - NxStage Cartridge CAR-170 with pre-attached dialyser
    - NxStage Cartridge CAR-171 with pre-attached dialyser and heparin line
    - NxStage Cartridge CAR-172C with pre-attached dialyser and LockSite medication ports (the manufacturer states that this cartridge is used in 95% of cases in the UK)
    - NxStage Cartridge CAR-124 without pre-attached dialyser
    - NxStage Cartridge CAR-125B (available on a case-by-case basis for the paediatric population) without pre-attached dialyser
  - One of the following dialysers must be used. Dialysers are pre-attached to all types of cartridges except for CAR-124 and CAR-125B. For these cartridges, the physician must decide which dialyser to use for each patient. These stand-alone dialysers are manufactured by Asahi Kasei Medical.
    - Leoceed-N16
    - Leoceed-N21
    - Leoceed-H16
    - Leoceed-H21
- The PureFlow SL integrated system for purification of tap water.
- Dosing calculator software.

Description

The NxStage System One is a transportable haemodialysis device intended for use in the home or while travelling by adults and children suffering from stage 5 CKD. The device is operated using controls on the cycler user interface. The dialysis fluid for use with the NxStage System One can come from 2 sources. One option, mainly intended for use while travelling, is to use pre-packaged, pre-mixed sterile bags of PureFlow dialysis fluid that are heated to body temperature. There are 2 fluid warming systems that are compatible with

the NxStage System One. The Express Fluid Warmer is compatible with all NxStage Cartridges except CAR-124 and CAR-125. If CAR-124 or CAR-125 are used, the dialysis fluid must be heated with The Fluid Warming System. The second option is for preparing dialysis fluid, is to make it in the home using tap water that has been purified using the PureFlow SL system. This purified water is then mixed with PureFlow sterile dialysis concentrate to give 40–60 litres of dialysate, and this is warmed in the PureFlow SL before use. This option is intended for use in the home. For each dialysis session a pre-sterilised, single-use NxStage cartridge (listed above) is required. Cartridges CAR-170, -171 and -172C are pre-attached to a dialyser. Cartridges CAR-124 and -125B are not pre-attached to a dialyser and, therefore, a dialyser will need to be selected and then attached to the cartridge before each dialysis session. NxStage offers cartridges without pre-attached dialysers to increase clinician choice and flexibility of treatment.

The express fluid warmer sits on top of the cycler. All of the blood- and fluid-containing circuits are contained within the treatment cartridges, so there is no direct contact between the cycler and the blood or the fresh dialysate.

The NxStage System One measures 38 cm x 38 cm x 46 cm and weighs 33 kg. The manufacturer states that the NxStage System One is smaller than conventional haemodialysis machines, and unlike current conventional haemodialysis systems the device can function with standard mains electrical and water supplies without the need for conversion of domestic supplies. The waste fluid is disposed of down a standard drain.

NxStage Medical lists 5 models of the NxStage System One device, which can perform a range of treatment functions for both acute and chronic forms of kidney disease. According to the manufacturer, only the NX1000-1 model is available for use in the UK; in line with the scope of this briefing, the NX1000-1 model is intended for home haemodialysis for people diagnosed with CKD. The other models listed by the manufacturer are CE-marked but have not yet been officially launched in the UK.

Intended use

The NxStage System One is intended to provide haemodialysis in the home or while travelling, for people who have been diagnosed with stage 5 CKD. It is also indicated for the treatment of acute and chronic renal failure, or fluid overload using haemofiltration, haemodialysis, and/or ultrafiltration, in an acute or chronic care facility, but these uses are beyond the scope of this briefing.

Setting and intended user

NxStage Medical specifies in the NxStage System One User Guide and Instructions for Use that treatment with the NxStage System One must be prescribed by a clinician. In the UK, this may be either a doctor or a nurse independent prescriber. This treatment prescription will include:

- the frequency and duration of haemodialysis
- the cartridge model
- the concentration of dialysate electrolytes
- blood flow rates.

The manufacturer does not recommend use of the device unless users meet the following criteria:

- have a dedicated caregiver or partner who is receptive to continual training
- have stable vascular access
- have a high standard of hygiene within the home to prevent infection and ensure safety

Both the person having haemodialysis and an accompanying caregiver need in-depth training to use the device. NxStage Medical provides training for NHS staff, who in turn provide training to people who intend to have home haemodialysis with the NxStage System One. Training programmes are managed by the individual hospital departments. These can be tailored to match the needs of the person who will be having the treatment. For example, 2-week intensive courses have been used for people already established with haemodialysis, whereas 3- to 5-week programmes have been used for people who are new to haemodialysis.

The NxStage System One is intended for use in the home (or while travelling) to give greater flexibility to people needing RRT. The home environment also offers a more practical setting for changing treatment frequency compared with conventional in-centre haemodialysis regimes. Home haemodialysis regimes often use shorter and more frequent sessions of haemodialysis or alternate nocturnal regimes. Regimes are often personalised to suit the need of the individual.

Several features of the NxStage System One, such as the integrated water purification system, its compact size and pre-mixed dialysate fluids, are designed to allow home dialysis without needing significant changes to the home (Clark and Turk, 2004). The following facilities are needed for home dialysis with the NxStage System One:

- A reliable mains water and electrical source.
- Close access to a standard drain for waste disposal.
- Adequate storage for a 2-week supply of premixed dialysate or dialysis concentrate and consumables.
- Caution should be taken with babies, young children and pets, to reduce the chance of interference with the system and the subsequent risk of infection.

Current NHS options

NICE's technology appraisal guidance on home compared with hospital haemodialysis for patients with end-stage renal failure recommends that people with stage 5 CKD should have a detailed assessment to determine the appropriate treatment option. If haemodialysis is considered to be a suitable treatment, the person's clinical and psychological suitability and social circumstances should be assessed before home haemodialysis is considered. Specifically, NICE recommends that people considering home haemodialysis must have '1 or more carers who have also made an informed decision to assist with the haemodialysis' and who are given the opportunity to voice their opinions independently of the person wishing to start home haemodialysis. Alternatively, NICE recommends that if the person having treatment for CKD is able to take responsibility for their therapy in a proactive manner, they may be able to manage their care independently ('on his or her own'). However, NxStage Medical states that therapy should not, in any circumstance, be done without a caregiver.

People intending to have home haemodialysis with the NxStage System One should consider the impact on their home. A suitable amount of space is needed to house the machine and the additional consumables. All home users must maintain a high level of cleanliness to prevent infection, particularly if small children or pets are present. An additional cost in utility bills should also be considered.

NICE is not aware of other transportable haemodialysis devices which are designed to be used at home or while travelling, without modifications to the home water or electrical

supply.

Costs and use of the technology

The manufacturer did not provide a purchase price for the NxStage System One because it is negotiated on a cost-per-treatment basis. This cost varies depending on several factors, including the following:

- The level of service for which NHS Trusts contract. This can vary, depending on the arrangements for delivery of the NxStage products, or whether any drugs or ancillary items are purchased from NxStage Medical.
- The number of patients in the trust whose CKD is being treated using the NxStage System One. Tiered price discounts apply depending on the size of the patient group.
- The number of treatments needed per patient, per week.
- The volume of dialysate solution delivered per patient.

The manufacturer claims that across the range of programmes it offers, the price per treatment using the NxStage System One is approximately 60% of the current weekly NHS tariff cost for home haemodialysis. The 2014/15 weekly NHS tariff cost for home haemodialysis is £449 for adults aged 19 years and over. Alternative treatment options for dialysis and their associated costs are outlined in the table below (unit costs for each treatment from NHS Reference Costs 2012-13, represented as a weighted average based on the activity and unit cost per DRG code).

Dialysis treatment option	Cost per session
Hospital haemodialysis	£157.92
Satellite haemodialysis	£148.18
Home haemodialysis	£138.67
Peritoneal dialysis	£65.26

Likely place in therapy

The NxStage System One is likely to be used as a home-based treatment option for people

with stage 5 CKD who need RRT.

Specialist commentator comments

All specialist commentators who reviewed this briefing felt that the NxStage System One could be used by people who do not have the support of a caregiver in their home. This is in disagreement with the manufacturer's criteria, which specifically exclude people who do not have a dedicated caregiver from using the NxStage System One.

The specialist commentators noted that additional training and specific safety measures could be put in place so that a person using this device without carer support could have access to immediate help should they need it. Two specialist commentators stated that people without caregivers who wished to have haemodialysis independently in the home had to sign a contract from the prescribing centre, confirming that they understood the risks of dialysing independently.

One of the specialist commentators noted that in addition to clinical end points, patient-centred outcome measures were particularly important in considering the NxStage System One. Three of the specialist commentators highlighted the observed quality of life improvements using NxStage System One, and reiterated that patient choice should be prioritised. In general, specialist commentators noted that people who were given the opportunity to take control of their RRT using the NxStage System One described a positive effect on their quality of life.

The specialist commentators noted that the device's ease of use and flexibility meant that more people would be eligible for home haemodialysis. Furthermore, the simple user interface has made the NxStage System One a successful option for children and, as a result, children have been able to return to full-time education and go on holiday, which are factors not necessarily considered in outcome measures in clinical studies. These factors are limited in the case of conventional haemodialysis, in-centre or at home.

Two specialist commentators described their experiences of successfully using the NxStage System One in combination with adapted dialysis cartridges for treatment of CKD in children from 3 years of age and weighing less than 15 kg. They used the CAR-124 cartridge and the CAR-125B cartridge. Both these cartridges need to be attached to a separate dialyser, as selected by the physician, in order to function.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. We aim to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women, and
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief, in the way we produce our guidance (these are protected characteristics under the Equality Act 2010).

The NxStage System One is intended for people with stage 5 CKD. As a chronic condition, this is considered a protected characteristic as defined by the Equality Act (2010).

Home haemodialysis using the NxStage System One may improve quality of life outcomes. The treatment flexibility offered by the system may allow people using it to adjust their haemodialysis schedule around their work, school and social activities.

Jehovah's Witnesses may be opposed to haemodialysis (using any of the available technologies) because of their belief that blood should not be removed from the body.

The manufacturer states that users must have a dedicated caregiver who is willing and capable to have training on the use of the NxStage System One. Reliable access to mains electricity and water, adequate storage for a 2-week supply of dialysis consumables, and access to a standard drain are also necessary. If these criteria cannot be met then physicians may choose to exclude these patients from using the NxStage System One.

Patient and carer perspective

The British Kidney Patient Association (BKPA) made the following comments on the device.

Flexible dialysis treatments such as the NxStage System One increase the likelihood of people using dialysis being able to return to work and to travel, which would improve their quality of life. However, nocturnal home dialysis can have a negative impact on quality of life: the machines can be noisy and this can stop the person having dialysis (and

potentially their partner) from sleeping. Home dialysis can also make the user feel isolated because they are not in such regular contact with medical professionals, and so it is important that people having dialysis at home are not ignored. NxStage Medical suggests that respite programmes and continual consultation with health care professionals may help to mitigate this risk.

The BKPA highlighted that the needs of the carer should not be overlooked, and so they should be offered support. It noted that some people who do not have a caregiver at home may still choose to use home haemodialysis, although NxStage Medical states that users must have a caregiver in the home in order to use this system. Caregivers may become ill, making it difficult for them to assist the person using dialysis; this eventuality should be taken into consideration.

Finally, the BKPA highlighted the gap in the research literature concerning home haemodialysis and emphasised that both patient-reported outcome measures and patient-reported experience measures should be presented, in addition to clinical outcome measures.

The NICE Public Involvement Programme team highlighted additional equality considerations for people with visual impairment or learning difficulties who may be not be able to use home haemodialysis with the NxStage System One without additional support. People without a fluent grasp of English may also be excluded because of an inability to train continually without the help of an interpreter. However, the manufacturer states that its user guides are available in different languages.

Evidence review

Clinical and technical evidence

Nine publications reporting upon the findings of 7 clinical studies were included in this briefing.

The publications by Finkelstein et al. (2012), Jaber et al. (2011) and Jaber et al. (2010) all report outcomes of the FREEDOM study (Following Rehabilitation, Economics And Everyday-Dialysis Outcome Measurements) at different time-points (see protocol outline by Jaber et al. 2009). The study by Munshi et al. (2013) was the only relevant study that had been published in abstract form only.

The 7 clinical studies ranged from single-centre feasibility studies to prospective multicentre cohort studies. Table 1 summarises all the selected studies with their corresponding publications and their basic characteristics.

Table 1 Summary of identified studies characteristics

Study	Population	Number of people	Haemodialysis schedule	Comparator	Design	Manufact funding f study
FREEDOM study interim report (Finkelstein et al. 2012)	Adult	291*	Short daily	Baseline	Prospective/ cohort	Yes
FREEDOM study interim report (Jaber et al. 2011)	Adult	235*	Short daily	Baseline	Prospective/ cohort	Yes
FREEDOM study interim report (Jaber et al. 2010)	Adult	239*	Short daily	Baseline	Prospective/ cohort	Yes
(Weinhandl, Liu et al. 2012)	Adult	11,228	Daily	Matched-cohort	Retrospective/ matched cohort	Yes
(Goldstein et al. 2008)	Paediatric	4	Daily	Baseline	Prospective/ feasibility	Yes
(Zaritsky et al. 2014)	Adult	78	Short daily	Baseline	Unknown/ cross-sectional	No

(Munshi et al. 2013)	Not reported	973	Unknown	Peritoneal dialysis	Unknown/ cohort	Not state
(Kohn et al. 2010)	Adult	5	Short daily	Baseline	Unknown/ feasibility	No
(Kraus et al. 2007)	Adult	25	Daily	Baseline	Prospective/ cross-over feasibility	Yes
* Interim outcome reports of the FREEDOM study. These are cumulative recruitment figures of th same patient cohort, with the most recent being from Finkelstein et al. (2012).						

Pilot and feasibility studies

Three feasibility studies (Kohn et al. 2010; Goldstein et al., 2008; Kraus et al. 2007) and 1 cross-sectional study (Zaritsky et al. 2014) reported on initial safety and efficacy findings using the NxStage System One in home haemodialysis. Kohn et al. (2010) studied the effectiveness of the NxStage System One for metabolic waste product removal from the blood in 5 people having short home haemodialysis sessions 6 times per week. In terms of short daily low flow rate, the NxStage System One (used 6 days per week for an average of 17.5 hours per day, over 8–16 months) was equally effective as conventional haemodialysis (used 3 times per week for 4 hours per session). This was measured by the removal of beta 2 microglobulin, phosphorus and urea nitrogen waste products from the blood (table 2).

Goldstein et al. (2008) studied the feasibility of haemodialysis with the NxStage System One in a small paediatric population (n=4) over 16 weeks of treatment. They reported no serious adverse events and concluded that frequent haemodialysis with the NxStage System One is feasible for children who would benefit from home haemodialysis (table 3).

Kraus et al. (2007) conducted a 2-month crossover feasibility study of 25 people using the NxStage System One for in-centre followed by at-home haemodialysis. They concluded that the system offers a viable dialysis option for people with stage 5 CKD who are capable of home haemodialysis. There was a statistically significant increase in the number of adverse events recorded per 100 treatments in people having dialysis in-centre compared with at home dialysis. Adverse events in more than 1% of the treatments were blood under-heating, muscle cramping, hypotension, headache, dizziness and fatigue (see

table 4).

In their cross-sectional study, Zaritsky et al. (2014) analysed the following outcomes in 24 people having short daily haemodialysis using the NxStage System One compared with 54 people having conventional in-centre haemodialysis:

- Standardised Kt/V (a measure of renal dialysis adequacy).
- The level of fibroblast growth factor 23 in the plasma.
- Haematocrit and serum albumin levels.
- Blood calcium, phosphorus and intact parathyroid hormone levels.
- The use of vitamin D, calcimimetic and phosphate binder.

Most of these biochemical parameters did not differ between people using the 2 haemodialysis methods (table 5).

Large cohort studies

The FREEDOM study is a prospective, multicentre, observational cohort trial sponsored by NxStage Medical. The study includes people covered by Medicare health insurance who convert to daily home haemodialysis with the NxStage System One. The target sample size is 500 people. At the time of writing the study is reported to be completed, although full results have not yet been published.

To date, 3 interim reports of the FREEDOM Study have been published: Jaber et al. (2010) reports on experiences of depressive symptoms (table 6); Jaber et al. (2011) reports on experiences of restless leg syndrome (table 7) and Finkelstein et al. (2012) reports on quality of life measures (table 8).

A matched-cohort retrospective study by Weinhandl et al. (2012) provides the only published evidence comparing survival rates between standard in-centre and daily home haemodialysis using the NxStage System One. The authors report that in a cohort of 11,228 people with stage 5 CKD, daily home haemodialysis was associated with modest improvements in survival relative to standard three times-weekly in-centre haemodialysis (table 9).

The single-centre study by Munshi et al. (2013) analysed patient survival and technique survival (the time between starting 1 renal replacement therapy and switching to another) in people using home haemodialysis compared with people using peritoneal dialysis. The authors reported the experience of 236 people having home haemodialysis using the NxStage System One, compared with 737 people having peritoneal dialysis, over 7 years (from 2004 to 2011). The study concluded that both treatment methods provided similar patient survival, but that technique survival was better for home haemodialysis with the NxStage System One compared with peritoneal dialysis (table 10).

Table 2 Summary of the Kohn et al. (2010) single-centre feasibility study

Study component	Description
Objectives/ hypotheses	To study the effectiveness of the NxStage System One for blood waste product removal in patients having short daily home haemodialysis.
Study design	A single-centre feasibility study. The prospective or retrospective design of this study could not be verified from the publication.
Setting	USA-based. Study duration was 8 to 16 months. No information was provided on follow-up schedule.
Inclusion/ exclusion criteria	Inclusion criteria: patients having short home haemodialysis 6 times per week; aged 18 or older; with no residual renal function (defined as a urine output <100 mL/day).
Primary outcomes	B2M and urea clearance; phosphorus and potassium removal.
Statistical methods	Descriptive analysis, Pearson's correlation analysis, linear regression analysis.
Participants	5 patients, 4 of African-American family origin and 1 of Chinese-American family origin. Patient ages were not reported.

Results	Descriptive analysis: Weekly B2M, phosphorus and urea nitrogen compared favourably with published values from short daily and 3 times-weekly conventional haemodialysis done with machines using much higher dialysate flow rates. To achieve this result an average of 17.5 hours of dialysis per week was needed.
Conclusions	Short daily low flow rate with NxStage System One was equally effective as 3 times-weekly conventional haemodialysis in removing B2M, phosphorus and urea nitrogen waste products.
Abbreviations: B2M, beta 2 microglobulin.	

Table 3 Summary of the Goldstein et al. (2008) prospective feasibility study

Study component	**Description**
Objectives/ hypotheses	To demonstrate the feasibility of haemodialysis with the NxStage System One in a paediatric population during 16 weeks of treatment.
Study design	A prospective, multicentre feasibility study.
Setting	2 USA-based centres. Follow-up was at 2, 4, 8, 12 and 16 weeks after the initiation of NxStage System One. Study duration was 16 weeks.
Inclusion/ exclusion criteria	Patients having 3-times weekly haemodialysis for at least 2 consecutive months without a change in haemodialysis prescription; weighing >35 kg; and with no active inflammatory process, including infection or systemic inflammatory disease.

Primary outcomes	Primary outcome: feasibility of using the NxStage System One. Secondary outcomes: impact of the NxStage System One on: • post-dialysis target weight (kg) • standard Kt/V • serum electrolytes • blood pressure • serum cytokines • normalised protein catabolic rate nutritional • health-related quality of life parameters.
Statistical methods	No formal sample size calculation was done. Investigators only reported raw data for each trial participant, except for changes in cytokine levels, which was statistically analysed using ANOVA.
Participants	4 patients enrolled, 3 of whom had frequent haemodialysis at home and 1 of whom had in-centre dialysis. Weight range was 38.0–61.4 kg and body surface area range was 1.27–1.60 m^2. Causes of CKD were focal segmental glomerulosclerosis, immune complex glomerulonephritis, membranoproliferative glomerulonephritis type II and bilateral renal dysplasia.

Results	All 4 patients completed the 16-week study period. Changes were observed in: • pro-inflammatory cytokine levels (variable changes observed) • reduction in blood pressure compared to pre-treatment systolic and diastolic values • reduction in mean serum phosphorus. No change was observed in: • mean patient weight • nPCR • levels of serum albumin • levels of serum electrolytes • levels of haematocrit • HRQOL. No adverse effects were reported.
Conclusions	Frequent haemodialysis with the NxStage System One is feasible for children who would benefit from home-based maintenance dialysis.
Abbreviations: ANOVA, analysis of variance; CKD, chronic kidney disease; nPCR, Normalised Protein Catabolised Rate; HRQOL, Health-Related Quality of Life; standard Kt/V, a measurement of renal dialysis adequacy.	

Table 4 Summary of the Kraus et al. (2007) prospective crossover study

Study component	Description
Objectives/ hypotheses	To demonstrate the safety and efficacy of home-based daily haemodialysis compared with standard centre-based haemodialysis with the NxStage System One.

Study design	A prospective, multicentre, open-label, crossover, feasibility study.
Setting	Patients were recruited between February and November 2004 at 6 USA-based sites. Follow-up was at 2, 4 and 8 weeks of the in-centre and home phases.
Inclusion/ exclusion criteria	Inclusion criteria: life expectancy >1 year; haemodialysis at least 3 times weekly for a minimum of 3 months; an identifiable caregiver; >18 years old; vascular access capable of a minimum blood flow rate of 350 mL/ min, and capable of receiving a delivered single-pool Kt/V of 0.45 in ≤3.5 hours. Exclusion criteria: estimated GFR>46 mL/min/1.73 m^2 as estimated by 24-hour urine in the presence of greater than 400 cm^3 urine in 24 hours; liver disease; uncontrolled hypertension; symptomatic intradialytic hypotension; haemoglobin <10 g/dL; active infectious or inflammatory disease; documented noncompliance; and malignancy other than superficial skin carcinomas.
Primary outcomes	The primary efficacy end point was the ability to deliver ≥90% of the clinically prescribed dialysis volume. The primary safety end point was the composite measure of intra- and inter-dialytic adverse events, defined as any unfavourable or unintended sign, symptom or disease temporally associated with use of the device. Secondary end points were: • delivered single-pool urea Kt/V per treatment • KDQoL Short Form • successful completion of the training programme by the patient and their caregiver • clinical utility (defined as usability) of the NxStage System One • ability to achieve target net ultrafiltration volume per treatment.

Statistical methods	Formal sample size calculation (including the drop-out of 10 patients) of 35 patients to detect a difference between treatment groups for the primary end point as well as the adverse event rates. The primary efficacy end point was compared between the 2 treatment environments (in-centre and home) using a generalised linear model with GEE. Retrospective descriptive analysis of patients' medical records for baseline comparisons between in-centre and home treatment parameters. All significance tests calculated for $p<0.05$. No adjustments were made for multiple comparisons.
Participants	Of the 32 patients enrolled, 25 completed the study. Mean age was 51 years, ranging from 18 to 71 years; 63% were men. Patient ethnicities were reported as: 75% were white, and 19% were of black or African-American family origin. The primary aetiology for renal disease was diabetes, hypertension, glomerulonephritis, polycystic disease and other.
Results	Successful delivery of at least 90% of prescribed fluid volume (primary end point) was achieved in 98.5% of treatments in-centre and 97.3% at home. Total effluent volume as a percentage of prescribed volume was 94–100% for all study weeks. The composite rate of intra- and inter-dialytic adverse events per 100 treatments was significantly higher for in-centre (5.30) compared with home (2.10; $p=0.007$). Compared with immediately before the study, there were reductions in blood pressure, antihypertensive medications and interdialytic weight gain.
Conclusions	Daily home haemodialysis with a small, easy-to-use haemodialysis device was found to be a viable dialysis option for patients with stage 5 CKD capable haemodialysis that was either self-administered or administered by a caregiver.
Abbreviations: CKD, chronic kidney disease; GEE, generalised estimated equations; KDQoL, Kidney Disease Quality of Life.	

Table 5 Summary of the Zaritsky et al. (2014) non-randomised, cross-sectional study

Study component	Description
Objectives/ hypotheses	To compare the levels of FGF23 and other biochemical variables in patients having short daily haemodialysis using the NxStage System One and in patients having conventional in-centre haemodialysis.
Study design	A multicentre, non-randomized cross-sectional study. The prospective or retrospective design could not be verified from the publication.
Setting	Patients were recruited between January 2009 and January 2012 at 2 USA-based centres. Biochemical measurements were taken immediately before dialysis treatment (48 hours after the prior treatment in the conventional group and 24 hours after the prior treatment in the short daily haemodialysis group). No information was provided on follow-up schedule.
Inclusion/ exclusion criteria	Inclusion criteria: aged 18–80 years; having had conventional maintenance dialysis and short daily haemodialysis for > 3 months. No information was provided on exclusion criteria.
Primary outcomes	Impact of the NxStage System One on: • haematocrit levels • std Kt/V • albumin, calcium and phosphorus levels • iPTH • FGF23 • vitamin D, calcimimetic and phosphate binder use.
Statistical methods	No formal sample size calculation was done. The authors have a descriptive analysis of the outcomes, and did Spearman correlation and linear regression. No adjustment for multiple comparisons was made.

Participants	54 patients having conventional haemodialysis and 24 having short daily haemodialysis with the NxStage System One, aged 60.8±2.6 and 45.3±4.7 years ($p<0.05$) respectively. Median dialysis treatment length was 2.4 years (interquartile range 1.2, 4.1) for the people having conventional haemodialysis and 2.8 years (1.1, 7.6) for people using the NxStage System One.
Results	No statistical difference was seen in Kt/V, haematocrit, calcium, phosphorus, and PTH concentrations. Statistical differences were seen in serum albumin (lower in the conventional haemodialysis group) and plasma FGF23 values (lower in the short daily haemodialysis cohort). No association was seen between length of dialysis and FGF23 levels in either group. Phosphorus levels correlated with FGF23 concentrations in both groups ($r=0.42$, $p<0.01$ and $r=0.52$, $p<0.01$).
Conclusions	FGF23 levels were significantly lower in patients undergoing short daily haemodialysis with the NxStage System One. Other biochemical parameters were not affected by the modality of treatment.
Abbreviations: FGF23, fibroblast growth factor 23; iPTH; intact-parathyroid hormone.	

Table 6 Summary of the Jaber et al. (2010) interim report of the FREEDOM prospective cohort study

Study component	Description
Objectives/ hypotheses	To compare changes in depressive symptoms and post-dialysis recovery time in patients before and after changing their treatment from in-centre haemodialysis, peritoneal dialysis or kidney transplant, with home haemodialysis using the NxStage System One.
Study design	Prospective, multicentre, observational cohort study.
Setting	Patients were recruited between January 2006 and December 2008 at 28 USA-based sites. Follow-up was at 4 and 12 months after initiation of short daily haemodialysis.

Inclusion/ exclusion criteria	Inclusion criteria: diagnosis of stage 5 CKD needing dialysis; Medicare as the primary payer; candidate for daily haemodialysis (defined as dialysis 6 or more times per week); ability to understand and willingness to sign an informed consent statement and a Health Insurance Portability and Accountability Act of 1996 compliant authorization statement. Exclusion criteria: current use of the NxStage System One haemodialysis device; previous enrolment in this study; current enrolment in another investigational drug or device trial which might impact the outcome measures planned in this study; likelihood of not surviving the training period.
Primary outcomes	Interim report from the FREEDOM study presenting the secondary outcomes of depressive symptoms (as measured by the BDI) and post-dialysis recovery time as measured by a special study question: "How long does it take you to recover from a dialysis session and resume your normal, usual activities?"
Statistical methods	• Formal sample size calculation (30% drop-out rate) of 25 and 55 patients (for BDI score and time to recovery respectively) performed for the 12-month time point to achieve 80% power with type I error of 0.05 (based on a mean improvement of 8±10 units and 100±150 minutes respectively). • Per protocol (patients with 12-months' follow-up completion only. • ITT analysis (all patients). • Sensitivity analysis. • Multiple comparisons adjustment*.
Participants	239 patients were enrolled (ITT cohort) and 128 completed the study (per-protocol cohort). Mean age was 52 years, 64% were men, 55% had an arteriovenous fistula (the others had arteriovenous grafts or central venous catheters) and 90% transitioned from in-centre haemodialysis (the others transitioned from peritoneal dialysis, kidney transplant or were new to RRT).

Results	Per protocol cohort (n=128): significant decrease in mean BDI score (11.2 [95% CI 9.6 to 12.9] vs 7.8 [95% CI 6.5 to 9.1]; p<0.001). Significant decrease in mean post-dialysis recovery time over 12 months (476 [95% CI 359 to 594] vs 63 minutes [95% CI 32 to 95] p<0.001). ITT analysis (n=239) showed similar results. The results remained significant after sensitivity analysis.
Conclusions	Daily haemodialysis with the NxStage System One was associated with long-term improvement in depressive symptoms and post-dialysis recovery time.
Abbreviations: BDI, Beck Depression Inventory; ITT, intention to treat; RRT, renal replacement therapy. * According to the original study protocol, multiple comparisons adjustment would be performed. This could not be subsequently verified in the interim reports' statistical methods and results description.	

Table 7 Summary of the Jaber et al. (2011) interim report of the FREEDOM prospective cohort study

Study component	Description
Objectives/ hypotheses	To compare changes in RLS and sleep disturbances in patients before and after conversion to the NxStage System One.
Study design	A prospective, multicentre, observational, cohort study.
Setting	Patients were recruited between January 2006 and December 2009 at 28 USA-based sites. Follow-up was 4 and 12 months after initiation of short daily haemodialysis.

Inclusion/ exclusion criteria	Inclusion criteria: diagnosis of stage 5 CKD needing dialysis; Medicare as the primary payer; candidate for daily haemodialysis (defined as dialysis 6 or more times per week); ability to understand and willingness to sign an informed consent statement and a Health Insurance Portability and Accountability Act of 1996 compliant authorization statement. Exclusion criteria: current use of the NxStage System One haemodialysis device; previous enrolment in this study; current enrolment in another investigational drug or device trial which might impact the outcome measures planned in this study; likelihood of not surviving the training period.
Primary outcomes	Interim report from the FREEDOM study, presenting the secondary outcomes of: presence and severity of RLS, assessed at enrolment then at 4 and 12 months using the IRLS Study Group Rating Scale (version 2.2); and presence and severity of sleep disturbances.
Statistical methods	• Formal sample size calculation (30% drop-out rate) of 43 patients done for the 4- and 12-month time points to achieve 80% power with a type I error of 0.05. • The sample size was calculated on the basis of a mean IRLS global score improvement of 6±9 (SD) units. • Per protocol and ITT analysis. • Sensitivity analysis. • Multiple comparisons adjustment*.
Participants	235 patients with stage 5 kidney disease having daily home haemodialysis with the NxStage System One. Mean age was 52 years, 65% were men, 66% were white, 43% had diabetes, and 55% had an arteriovenous fistula.
Results	Per-protocol analysis: mean IRLS score improved significantly. ITT analysis: decline in the percentage of patients reporting RLS (35% vs 26%), and moderate-to-severe RLS (59% vs 43%). Similar and sustained 12-month improvement in several scales of the sleep survey.

Conclusions	Short daily home haemodialysis was associated with long-term improvement in the prevalence and severity of RLS and sleep disturbances.
Abbreviations: ITT, intention to treat; RLS, restless legs syndrome; IRLS, International Restless Leg Scale. * According to the original study protocol multiple comparisons adjustment would be performed. This could not be subsequently verified in the interim reports' statistical methods and results description.	

Table 8 Summary of the Finkelstein et al. (2012) interim report of the FREEDOM prospective cohort study

Study component	Description
Objectives/ hypotheses	To compare changes in quality of life measures in patients before and after conversion to the NxStage System One device.
Study design	A prospective, multicentre, observational, cohort study.
Setting	Patients were recruited between January 2006 and December 2009 at 33 USA-based sites. Follow-up was done 4 and 12 months after initiation of short daily haemodialysis.
Inclusion/ exclusion criteria	Inclusion criteria: diagnosis of stage 5 CKD needing dialysis; Medicare as the primary payer; candidate for daily haemodialysis (defined as dialysis 6 or more times per week); ability to understand and willingness to sign an informed consent statement and a Health Insurance Portability and Accountability Act of 1996 compliant authorization statement. Exclusion criteria: current use of the NxStage System One haemodialysis device; previous enrolment in this study; current enrolment in another investigational drug or device trial which might impact the outcome measures planned in this study; likelihood of not surviving the training period.
Primary outcomes	Interim report of the FREEDOM study, presenting the secondary outcomes of health-related quality of life as measured by the SF-36 health survey.

Statistical methods	• Formal sample size calculation (30% drop-out rate) of 153 patients was done at 4 and 12 months to achieve 80% power with type I error of 0.05. • As-treated analysis (patients with 12 months' follow-up completion only) and total cohort analysis (all patients). • Sensitivity analysis. • Multiple comparisons adjustment*.
Participants	312 patients were enrolled and 291 completed the survey. Mean age was 53 years, 66% were men, 70% were white, 45% had diabetes, 90% had hypertension, 27% had a history of congestive heart failure and 58% had an arteriovenous fistula.
Results	Total cohort analysis (n=291): both the physical and mental summary scores improved, as did all 8 individual domains of the SF-36. As-treated cohort analysis (n=154): similar improvements with the exception of the role-emotional domain. The results remained significant after sensitivity analysis.
Conclusions	At-home short daily haemodialysis with NxStage System One was associated with long-term improvements in various physical and mental health-related quality of life measures.
* According to the original study protocol multiple comparisons adjustment would be performed. This could not be subsequently verified in the interim reports' statistical methods and results description.	

Table 9 Summary of the Weinhandl et al. (2012) retrospective matched-cohort study

Study component	Description
Objectives/ hypotheses	To assess mortality in patients having daily home haemodialysis with the NxStage System One and a matched-cohort having 3 times-weekly in-centre haemodialysis.

Study design	A retrospective, multicentre, observational, matched-cohort study.
Setting	Patients were recruited over 2005–08 across an unspecified number of sites in the USA. Matched in-centre patients were identified from the US Renal Data System database (637,109 records). Daily haemodialysis patients were identified from a registry of NxStage System One users maintained by NxStage Medical (2816 records). Follow-up was done until December 2008.
Inclusion/ exclusion criteria	Matching method: • Medicare as primary payer. • To have begun RRT during the 6 preceding months. • Subsequently matching according to 17 factors: age, cumulative hospital days, cumulative EPO dose, BMI, transplant waitlist registration, congestive heart failure, CKD duration, race, cancer, primary CKD cause, cerebrovascular disease, peripheral vascular disease, other cardiovascular disease, diabetes, atherosclerotic heart disease, sex and dual Medicare/Medicaid eligibility. • For each daily haemodialysis patient, 5 three times-weekly in-centre patients with matching characteristics were selected.
Primary outcomes	Mortality rate.

Statistical methods	No formal sample size calculation was done. • Descriptive analysis: match quality was assessed with standardised differences, with differences <10% indicating similarity. • Survival analysis: Kaplan–Meier method with both ITT and as-treated analyses. • Cox regression, with and without model-based adjustment for factors already included in the matching algorithm. • Discontinuation analysis: discontinuation of follow-up before December 2008. • No multiple comparisons adjustment was done. • Sensitivity analysis: performed on the ITT all-cause mortality HR with adjustment for an unmeasured hypothetical factor U.
Participants	1863 patients on daily haemodialysis with NxStage System One; 9365 on in-centre thrice weekly dialysis. Patients having daily haemodialysis were younger (mean age 52.2 versus 62.6 years), more frequently wait-listed for kidney transplant (35.0% versus 14.2%), had lower incidence of congestive heart failure (26.9% versus 44.6%), and had a lower proportion of people of African-Caribbean family origin (26.5% versus 38.8%).

Results	• All survival estimates between the 2 cohorts were statistically significant in favour of daily home haemodialysis. • The cumulative incidence of death was 19.2% among the patients having home haemodialysis and 21.7% among the in-centre patients respectively. • ITT analysis: home haemodialysis was associated with a 13% lower risk for all-cause mortality than in-centre haemodialysis (HR=0.87, 95% CI 0.78 to 0.97). • Cause-specific mortality HRs were 0.92 (95% CI 0.78 to 1.09) for cardiovascular disease, 1.13 (95% CI 0.84 to1.53) for infection, 0.63 (95% CI 0.41 to 0.95) for cachexia/dialysis withdrawal, 1.06 (95% CI 0.81 to 1.37) for other specified cause, and 0.59 (95% CI 0.44 to 0.79) for unknown cause. • As-treated analysis: similar findings to ITT. • No differences were detected from subgroup analyses. • Discontinuation analysis: 626 (39.5%) and 1355 (17.1%) events occurred in daily home haemodialysis and matched in-centre patients respectively. • Reason-specific discontinuation HRs for daily home haemodialysis versus matched in-centre patients were 10.4 (95% CI 8.9 to 12.3) for change in dialytic modality, 1.06 (95% CI 0.89 to 1.25) for kidney transplant, and 0.92 (95% CI 0.68 to 1.26) for cessation of Medicare primary payer status. • In patients having daily home haemodialysis, significant predictors of change in dialytic modality included CKD duration at haemodialysis initiation (HR 0.98 per year), dual Medicare/Medicaid eligibility (HR 1.67), and any hospitalisation during the 3 months preceding initiation (HR 1.51). • Of patients having daily home haemodialysis who changed dialytic modality, 96.9% initiated in-centre haemodialysis and 3.1% initiated peritoneal dialysis.

	• Sensitivity analysis: only a strong unmeasured confounder (for example with HR=0.8 and prevalence difference ≥60%) could alone undo the observed association of daily home haemodialysis with mortality.
Conclusions	Relative to standard 3-times weekly in-centre haemodialysis, daily home haemodialysis was associated with modest improvements in survival.
Abbreviations: CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio; ITT, intention to treat; RRT, renal replacement therapy.	

Table 10 Summary of the Munshi et al. (2013) single-centre cross-sectional study

Study component	Description
Objectives/ hypotheses	To compare patient and technique survival amongst patients having home dialysis with NxStage System One and peritoneal dialysis.
Study design	No information on prospective/retrospective status, single-centre, cross-sectional study.
Setting	Patients were recruited between January 2004 and December 2011 across an unspecified number of sites in the USA. No information was provided on follow-up schedule.
Inclusion/ exclusion criteria	No information as this was presented in abstract form and not a full publication.
Primary outcomes	Patient survival rate and technique survival.

Statistical methods	• No formal sample size calculation was done. • Patient and technique survival rates were calculated using the actuarial method and standard error and statistical significance were calculated using Greenwood's formula. 8-year aggregate data were calculated as cumulative proportion surviving. • Calculations for technique survival were performed with and without using transplant as technique failure.
Participants	236 patients having home haemodialysis with the NxStage System One and 737 patients having peritoneal dialysis.
Results	Patient survival was similar for home haemodialysis and peritoneal dialysis (8-years: 40.3±5.2% and 38.0±3.5% for home haemodialysis and peritoneal dialysis respectively, p = 0.71). 8-year technique survival was lower for peritoneal dialysis than home haemodialysis, whether transplant was considered a technique failure (12.7±2.5% and 4.2±0.7% for home haemodialysis and peritoneal dialysis respectively, p<0.001) or not (36.9±5.0% and 13.1±1.7% for home haemodialysis and peritoneal dialysis respectively, p<0.001).
Conclusions	Both home dialysis therapies provided similar patient survival rates. Although shown to be better than in previously published data, technique survival with peritoneal dialysis was lower than that for home haemodialysis dialysis.

During the preparation of this briefing, 2 ongoing trials and 1 unpublished completed trial using the NxStage System One were identified:

- NCT00667511: Comparing nocturnal haemodialysis and short daily haemodialysis using the NxStage System One.
- NCT01062984: Comparing continuous venovenous hemofiltration versus continuous venovenous haemodialysis in acute kidney injury.
- NCT00633308: Phosphorus and calcium removal during long haemodialysis treatment sessions.

Costs and resource consequences

In the UK, 1080 people used home haemodialysis in 2011-2012 (Fogarty and Cullen, 2013) and this represents the population who could consider the NxStage System One as a treatment option within the NHS. The system is currently available in a number of NHS trusts, although no information on the exact number of hospitals using NxStage System One could be obtained from the manufacturer.

No change to the organisation or delivery of current treatment services would be needed. People wishing to undertake home haemodialysis using the NxStage System One will be required to take active responsibility for its use and for in-depth training to use the system.

No published evidence on resource consequences of the NxStage System One was identified in the systematic review of evidence. Economic analyses of the NxStage System One are planned to be included in the full results of the FREEDOM study which, at the time of writing, have yet to be published.

Strengths and limitations of the evidence

The evidence considered in this briefing ranged from small feasibility studies to large prospective and retrospective high quality cohort studies. No randomised controlled trials were identified.

The majority of health-related quality of life evidence was presented in the published interim analysis reports of the FREEDOM study, provided by Finkelstein et al. (2012), Jaber et al. (2011) and Jaber et al. (2010). Strengths of the FREEDOM study were the repeated measures at 4 and 12 months after starting to use the NxStage System One, its multicentre prospective design, the use of validated health questionnaires such as the SF-36 and Beck Depression Inventory health surveys, the sample size calculations for the primary and secondary outcomes, and the prospective multicentre study design. The findings of the study were strengthened because the intention-to-treat, per protocol and sensitivity analyses all provided the same results. However, the observational study design could introduce potential bias and confounders.

The quality of life outcomes reported in the FREEDOM interim reports were secondary outcomes but this was nevertheless important information for people having renal replacement therapy. This is evidenced by the comments reported from people attending the 2013 UK Home Dialysis Summit, who said that their experience of home haemodialysis

was not given adequate consideration in the reporting of data on dialysis (Home Dialysis Summit 2013). It was suggested that patient experience measures should be given priority over more traditional measures of health-related outcomes. This highlighted the unmet need for patient-reported outcomes measures and patient-reported experience measures. Patient-reported outcomes may reflect the social benefits of home dialysis and support the current NHS focus on patient-centred care and decision-making.

The findings of the Weinhandl et al. (2012) study were strengthened because the sensitivity analysis verified the observed result on mortality. Nevertheless, although the matching procedure attempted to minimize all factors that could affect the reliability of the result, it could not account for all the possible differences between people who were using the NxStage System One and those who were using in-centre haemodialysis. As an example of this limitation in matching the patients across the 2 treatment groups, people using the NxStage System One were younger, more likely to be listed for kidney transplant, less likely to have congestive heart failure, and less likely to belong to minority ethnic groups than people who were not offered home-dialysis. The age difference could be explained by the matching method used, allowing people with up to 10 years age difference to be considered of similar age. Non-randomised studies and registries are at risk of selection bias, and this was a limitation for all of the included studies. People using the NxStage System One were likely to be younger, fitter and have fewer comorbidities than people having in-hospital dialysis.

Most studies reported in this briefing used a short daily haemodialysis schedule, and as a result it was difficult to directly compare the performance of NxStage System One to conventional in-centre treatment schedules.

Apart from the Weinhandl et al. (2012) and Munshi et al. (2013) studies, the studies described in this briefing reported results made on baseline comparisons only. The FREEDOM study aimed to compare the number of hospitalisations for people using NxStage System One with a group of 500 people using in-centre haemodialysis. These data will be valuable, but the full results of this trial were not available at the time of publication.

The NxStage System One is intended for use in both adults and children, yet very little clinical evidence exists for the safety and efficacy of the system in children. The only feasibility study available (Goldstein et al. 2008) was of limited value as it included only 4 patients. Additionally, Stronach et al. (2013a) reported their UK-based experience on a small case series of 3 children with dialyser-induced thrombocytopaenia when using the

gamma-sterilized PUREMA dialyser that was part of the standard NxStage circuit. These adverse reactions were resolved in all 3 people by changing the dialyser and circuit within the NxStage System One.

Although improved outcomes were reported in the 2 feasibility studies which investigated the transition from in-centre dialysis to home haemodialysis with NxStage System One, the designs of these studies were unclear. Specifically, in the study by Goldstein et al. (2008), a reduction in blood levels of phosphorus and cytokines was reported in users of the NxStage System One, but it was unclear whether the blood samples for these measurements were taken before or after a haemodialysis session. The study by Kraus et al. (2007) reported that at least 90% of the prescribed fluid volume was successfully delivered in 98.5% of treatments using in-centre haemodialysis compared with 97.3% of treatments using home haemodialysis. However, it was unclear whether the prescribed volume was the same between the 2 settings.

The matched cohort study (Weinhandl et al. 2012) used data from the NxStage registry so there was potentially some overlap between their patient cohort and the rest of the studies.

Recruitment and logistical challenges, presented not only in home haemodialysis but in other studies investigating alternative dialysis strategies in general, make it difficult to conduct large randomised clinical trials (Abdel-Kader and Unruh 2012). For example, in the Frequent Hemodialysis Network Nocturnal Trial, the randomisation of treatment assignment was an obstacle to recruitment because most people interested in this study wanted to be dialysed at home (Rocco et al. 2011). Additionally, the large number of variables in alternative dialysis regimens – such as dialysis session duration and frequency, diffusion and convection, blood and dialysate flow rates and dialysis prescription – means that large randomised clinical trials would be needed to provide reliable results. The subject of establishing the best research approach to evaluate alternative dialysis strategies is still a matter of ongoing debate (Van Biesen and Lameire 2013).

No studies were identified where the NxStage System One was compared with home haemodialysis using conventional equipment. Therefore, patient benefits reported in the studies included in this briefing could potentially be provided by any form of home haemodialysis. Frequent dialysis regimens can also be performed using conventional home haemodialysis equipment and so patient benefits related solely to frequency of dialysis would apply to both NxStage System One and conventional equipment.

Lastly, 4 of these 7 clinical studies were funded by the manufacturer and this introduced the potential of bias in the reporting of outcomes.

Relevance to NICE guidance programmes

The use of NxStage System One is not currently planned into any NICE guidance programme.

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Search strategy and evidence selection

Search strategy

Embase 1980 to 2014 Week 28, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present; searched 18 July 2014

For clinical evidence:

1. nxstage.mp.

2. portable hemodialysis.mp.

3. home hemodialysis.mp. or Hemodialysis, Home/

4. home haemodialysis.mp.

5. purema.mp.

6. end stage renal disease.mp. or Kidney Failure, Chronic/

7. renal replacement therapy.mp. or Renal Replacement Therapy/

8. kidney failure.mp. or Renal Insufficiency/

9. 6 or 7 or 8

10. 1 or 2 or 3 or 4 or 5

11. 9 and 10

12. limit 11 to english language

13. limit 12 to human

14. limit 13 to yr="1998 -Current"

15. limit 14 to humans

16. remove duplicates from 15

The Cochrane and DARE databases were searched using the following keywords:

- Any field: nxstage/OR
- Any field: portable hemodialysis/OR
- Any field: home hemodialysis

Evidence selection

- Total number of publications reviewed: 791
- Total number of publications considered relevant: 42 (27 full publications and 15 abstracts)
- Total number of publications selected for inclusion in this briefing: 9 (8 full publication and 1 abstract)
- Exclusion criteria: case studies, editorials, letters, reviews, animal studies, and non-English language studies, not using the NxStage System One for renal replacement therapy.

For economic evidence:

1. end stage renal disease.mp. or Kidney Failure, Chronic/

2. renal replacement therapy.mp. or Renal Replacement Therapy/

3. kidney failure.mp. or Renal Insufficiency/

4. 1 or 2 or 3

5. nxstage.mp.

6. portable hemodialysis.mp.

7. home hemodialysis.mp. or Hemodialysis, Home/

8. home haemodialysis.mp.

9. purema.mp.

10. 5 or 6 or 7 or 8 or 9

11. cost*.mp.

12. economic*.mp.

13. 11 or 12

14. 4 and 10 and 13

15. limit 14 to yr="1998 -Current"

16. limit 15 to english language

17. limit 16 to humans

18. remove duplicates from 17

Cochrane Database of Systematic Reviews: Issue 7 of 12, July 2014

Cochrane Central Register of Controlled Trials: Issue 6 of 12, June 2014

#1 end stage renal disease or chronic kidney failure or renal replacement therapy or kidney failure or renal insufficiency

#2 nxstage or portable hemodialysis or home hemodialysis or purema

#3 cost* or economic*

#5 #1 and #2 and #3

DARE (Database of Abstracts of Reviews of Effects), NHS EED (National Health Service Economic Evaluation Database), and HTA (Health Technology Assessment) databases

(end stage renal disease or chronic kidney failure or renal replacement therapy or kidney failure or renal insufficiency) AND (nxstage or portable hemodialysis or home hemodialysis or purema) AND (cost or economic) IN DARE, NHSEED, HTA FROM 1998 TO 2014

Evidence selection (economic evidence)

- Total number of full-text publications considered relevant: 0
- Total number of abstracts considered relevant: 262
- Number of duplicated abstracts: 4

- Total number of abstracts reviewed: 258
- Total number of publications selected for inclusion in this briefing: 0
- Exclusion criteria: case studies, editorials, letters, reviews, conference proceedings/ abstracts, animal studies, non-English language studies, not using the NxStage System One for renal replacement therapy.

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

Development of this briefing

This briefing was developed for NICE by King's Technology Evaluation Centre (KiTEC). The Interim Process & Methods Statement sets out the process NICE uses to select topics, and how the briefings are developed, quality assured and approved for publication.

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ISBN: 978-1-4731-0830-1