HEALTH TECHNOLOGY ASSESSMENT REPORT

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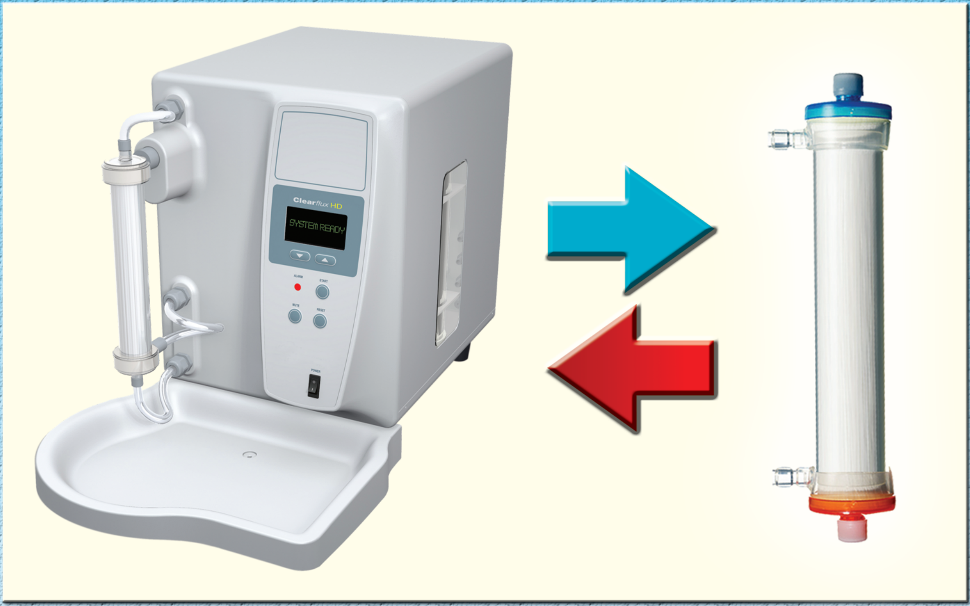
MINISTRY OF HEALTH MALAYSIA

SINGLE USE DIALYSER VERSUS REUSE DIALYSER



MaHTAS

Malaysian Health Technology Assessment Section

MEDICAL DEVELOPMENT DIVISION
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SINGLE USE DIALYSER VERSUS REUSE DIALYSER

DISCLAIMER

This Health Technology Assessment has been developed from analysis, interpretation and synthesis of scientific research and/or technology assessment conducted by other organisations. It also incorporates, where available, Malaysian data, and information provided by experts to the Ministry of Health Malaysia. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of the review.

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EXECUTIVE SUMMARY

Background

Renal replacement therapy in Malaysia has shown exponential growth since 1990. According to the 18th Report of The Malaysian Dialysis and Transplant Registry 2010, the number of dialysis patients in Malaysia has tripled in 10 years from 7,837 in 2001 to 21,245 in 2009. The number of haemodialysis centres for the whole of Malaysia increased from 208 in 2001 to 581 in 2010.In Malaysia, in 2010, 90% of patients undergoing haemodialysis were using reuse dialysers and 19% of patients used their dialysers for at least 13 times. About 80% of patients were using dialysers made from synthetic membrane. Dialyser reuse has historically been practised in light of perceived potential benefits for the dialysis provider and the patient. However, some of the original reasons are no longer valid. The availability of cheaper high-flux dialysers for single use means that the traditional benefit of the ability to reuse such dialysers no longer holds true. Potential errors and breakdowns in the reuse process are continuing concerns. The risk may move beyond bacteria into the realm of viruses and prions. In Ministry of Health (MOH) haemodialysis units, due to shortage of staffs, the dialyser reprocessing procedures are now performed by medical attendants. They are technically at risk of exposure to blood borne infections if adherence to standard precautions is not observed. It has been claimed that single use dialyser decreases rates of infection and contamination, likelihood errors and accidents, and risks associated with exposure to germicides and denatured blood products. Single use simplifies some of the operational aspects of haemodialysis and is convenient. The risk for medicolegal liability is also negligible in single use dialyser compared with reuse dialyser. Therefore, there is a need to reassess the dialyser reprocessing practice in MOH haemodialysis units.

Technical features

Haemodialysis is a method of removing waste products such as creatinine and urea, as well as free water from blood when the kidneys are in renal failure. The haemodialysis machine pumps the patient's blood and the dialysate through the dialyser. The dialyser is the piece of equipment that actually filters the blood. The dialyser may either be discarded after each treatment or be reused. There are two ways of reusing dialysers: manual reuse, and automated reuse by means of a medical device. A majority of facilities that reprocess dialysers are now using a peracetic acid mixture as the primary reuse reagent. The other reuse reagents include formaldehyde, glutaraldehyde and sodium hypochlorite. Dialyser membranes come with different pore sizes. Those with smaller pore size are called "low-flux" and those with larger pore sizes are called "high-flux". Dialyser membranes are made of modified cellulose or synthetic material.

Policy question

In MOH haemodialysis units, should single use dialyser be used for all haemodialysis patients or only for those with infectious diseases such as Hepatitis B, Hepatitis C, Hepatitis B & C co-infection or HIV infection?

Objectives

1. To assess the safety, effectiveness, economic implications, organizational, legal or environmental impacts of single use dialyser compared with reuse dialyser for haemodialysis of patients with end stage renal disease (ESRD) through a systematic review of the literature.(Part A)

2. To assess the cost-effectiveness of single use dialyser compared with reuse dialyser for haemodialysis of patients with ESRD in Malaysian public hospitals by conducting local economic evaluation.(Part B)

Methods

Part A (Systematic review of literature)

Studies were identified by searching electronic databases. The following databases were searched through the Ovid interface: MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R), EBM Reviews-Cochrane Database of Systematic Reviews, EBM Reviews-Cochrane Central Register of Controlled Trials, EBM Reviews–Database of Abstracts of Review of Effects, EBM Reviews-Health Technology Assessment, EBM Reviews-NHS Economic Evaluation Database, EMBASE 1988 to 2013 Week 09. Parallel searches were run in PubMed. No limits were applied to the search. The last search was run on 14 February 2013. Additional articles were identified from reviewing the references of retrieved articles. General search engine was used to get additional web-based information. Studies were selected based on inclusion and exclusion criteria. All relevant literature was appraised using the Critical Appraisal Skills Programme (CASP) tool. All full text articles were graded based on guidelines from the U.S./Canadian Preventive Services Task Force.

Part B (Local economic evaluation)

The economic evaluation was designed from the provider (Ministry of Health) perspective based on haemodialysis unit in general public hospital. The evaluation was conducted using Markov cohort analysis where the average five years' costs and consequences (quality adjusted life years, QALY) for the patient who received either type of dialyzer were evaluated. The model structure was simplified from a published Canadian model whereby patient who received single use/reuse dialyzer progress to either requiring transplant, or remaining in the dialysis state, or died within 1 year cycle. The cost and benefit was discounted at 3%.

Results and conclusion

Part A (Systematic review of literature)

A total of 180 abstracts were screened using the inclusion and exclusion criteria. After reading, appraising and applying the inclusion and exclusion criteria to 87 full text articles, 30 full text articles comprising one systematic review, two randomised controlled trials, three cross over design, five cohort studies, one pre and post-intervention study, 11 cross sectional studies, three case series, one cost-utility analysis, two cost analysis and one cost minimisation analysis, were finally included for this review.

Safety of single use dialyser versus reuse dialyser

- There was fair level of evidence to suggest:
  - Inadequate dialyser reuse practices were associated with outbreaks of bacterial infection and pyrogenic reactions.

  - Patients who reused dialysers were found to have 28% higher risk of septicaemia than patients who did not reuse dialysers and had a ninefold greater risk of death from septicaemia.

  - Reuse of dialyser was not associated with increased risk of HBV and HCV infection in either patients or staffs. However, (i) failure to identify and isolate HBV-infected patients during haemodialysis, (ii) sharing of staff, equipment, and supplies among patients, and (iii) failure to vaccinate susceptible patient were associated with outbreaks of HBV infection.

  - The incidence of new dialyser syndrome (first-use syndrome) has declined and was associated with regenerated cellulose and cuprophan membranes.

  - Reuse of hollow-fibre dialysers may be associated with anaphylactoid reactions.

- The evidence on intradialytic symptoms was inconclusive.

- The cumulative and long-term effects of chronic, low-dose exposure to reuse reagents (formaldehyde, hydrogen peroxide, sodium hypochlorite, glutaraldehyde and peracetic acid) cannot be determined.

Changes in membrane integrity

- There was fair to good level of evidence to suggest that small molecular weight solutes (urea, creatinine and phosphate) clearance were slightly greater for high- flux dialysers than low-flux dialysers. There was a trend for urea, creatinine and phosphate clearance to decrease with reuse for both high-flux and low-flux dialysers but these differences were not statistically significant.

- There was limited fair level of evidence to suggest that there was a small decline in dialysis dose (0.05 Kt/V units) when the mean frequency reuse was 3.8 to 13.8 times.

- There was fair to good level of evidence to suggest that clearance of large molecular weight solutes [β_2 Microglobulin (β_2M), retinol-binding protein (RBP)] was affected by reuse practices. β_2M clearance was low and not altered appreciably by reuse of low-flux dialysers. Clearance of β_2M was high for high-flux dialysers. However, clearance of β_2M and RBP for high-flux dialysers decreased with reuse. When bleach was included in germicide-based reprocessing cycles, β_2M clearances tend to increase. Eventhough the dialysers total cell volume (TCV) remained greater than 80%, reuse of high-flux dialysers does not ensure the maintenance of large solute clearance.

Clinical Effectiveness

- There was good level of evidence to suggest that there were no statistically significant differences in mortality between dialyser single use and dialyser reuse.

- There was fair level of evidence to suggest that reuse of dialysers was associated with higher hospitalisation rates from any cause. The higher rate of hospitalisation was observed with dialyser reuse using peracetic acid / acetic acid or formaldehyde.

Economic evaluation

- A cost-utility analysis performed in Canada in 2002 reported the cost saving that could be expected by switching from single use dialysis to heated citric acid reuse were small ranging from CAN $ 0 to CAN $ 739 per patient per year.

Organizational

- Reprocessing process entails multiple steps. Hence, personnel shall possess adequate education, training, or experience to understand and perform procedures outlined by the individual dialysis facilities.

- There was evidence to suggest that separation practices and ban on reuse of dialyser lower the incidence of Hepatitis B Virus or Hepatitis C Virus infection among patients.

Legal implication

- The requirement for reuse of dialyser in private healthcare facilities is included in the Malaysian Private Healthcare Facilities and Services Act 1998, Part XXII: Special requirements for haemodialysis facilities and services.

Environmental

- The dialysis procedure creates a considerable amount of waste (by single use or reuse practices). Hence, waste management needs to be part of dialysis provider system.

Part B (Local economic evaluation)

Single use was found to be more expensive but more effective than reuse. However, the incremental cost-effectiveness ratio (ICER) was found to be above the threshold of cost-effectiveness (MYR 4983655). The threshold of MYR 32,000 was used to determine the cost-effectiveness of the intervention at baseline. However, World Health Organization considered between one and three times gross domestic product (GDP) per capita as cost-effective. Threshold analysis showed that the breakeven point where both single use dialyser and reuse dialyser expected value are equal is MYR 1,418. Below this cost, the single use dialyser strategy would be favoured. It should be noted that the model has ignore possible effect of infectious disease contamination and associated building cost to accommodate high risk infected dialyser. Reuse seemed to be more cost-effective than single use dialyser.

Recommendation

Single use dialyser should be used for those with infectious diseases such as Hepatitis B, Hepatitis C, Hepatitis B & C co-infection or HIV infection, subjected to the availability of resource. Further economic evaluation using more complex model is advocated to determine the cost-effectiveness of using single use dialyser for all dialysed patients.

In line with the Ministry of Health guidance on Haemodialysis Quality and Standards and the Report of the Malaysian Dialysis & Transplant Registry where manual dialyser reprocessing system reported significantly higher risk for HCV seroconversion. Hence, automated reprocessing system for reuse of dialyser is advocated.

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ABBREVIATIONS

ESRD	End Stage Renal Disease
ESKD	End Stage Kidney Disease
WHO	World Health Organization
RRT	Renal replacement therapy
PMP	Per million population
HD	Haemodialysis
PD	Peritoneal dialysis
MOH	Ministry of Health
NGO	Non-governmental organization
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
CDC	Centers for Disease Control and Prevention
U.S.A.	United States of America
β2M	β2-microglobulin
U.S. FDA	United States Food and Drug Administration
USRDS	United States Renal Data System
AAMI	Association for the Advancement of Medical Instrumentation
TCV	Total cell volume
HFAK	Hollow fibre artificial kidney
ACE	Angiotensin-converting-enzyme
RCT	Randomised controlled trial
SR	Systematic review
OR	Odds ratio
HR	Hazard ratio
RR	Relative risk
CI	Confidence interval
SMR	Standardised Mortality Ratio
RR	Relative risk
mL	Millilitre
SMR	Standardized mortality ratio
SEM	Standard error of mean
SD	Standard deviation
ICER	Incremental cost-effectiveness ratio
QALY	Quality adjusted life years

HEALTH TECHNOLOGY ASSESSMENT

1 BACKGROUND

End stage renal disease (ESRD) or end stage kidney disease (ESKD) can be defined by the requirement for life-saving dialysis or kidney transplantation. According to the Bulletin of World Health Organization (WHO) 2007, worldwide the number receiving renal replacement therapy (RRT) which includes dialysis (haemodialysis and peritoneal dialysis) and kidney transplant is estimated at more than 1.4 million with incidence growing by approximately 8% annually. The increase is attributed to population ageing, type 2 diabetes mellitus and hypertension which are the key risk factors for chronic kidney disease. However, due to the expensive nature of RRT, treatment of ESRD is largely the domain of high income countries.[1]

Renal replacement therapy in Malaysia has shown exponential growth since 1990.[2-3] According to the 18th Report of The Malaysian Dialysis and Transplant Registry 2010, dialysis acceptance rates increased from 88 per million population (pmp) in 2001 to 170 pmp in 2009. Dialysis prevalence rate more than doubled over the last 10 years, from 325 pmp in 2001 to 762 pmp in 2009. The number of dialysis patients in Malaysia has tripled in 10 years from 7,837 in 2001 to 21,245 in 2009. The number of haemodialysis (HD) centres for the whole of Malaysia increased from 208 in 2001 to 581 in 2010 giving a rate of 9 pmp in 2001 and 21 pmp in 2010. The Ministry of Health (MOH) provided dialysis to 30% of patients, non-governmental organization (NGO) to 28% of patients and the private sector to 40% of all dialysis patients. Fifty seven percent of patients on dialysis were funded by the government, 10% by NGO, 22% were self funded, 1% subsidised by employer and 10% others. The proportion of new ESRD patients with diabetes was 56% in 2010. In contrast, peritoneal dialysis (PD) centres rate remained at 1 pmp through the last 10 years.[4] A cost-effectiveness evaluation of the MOH dialysis programme published in 1999 concluded that MOH dialysis programme was cost-effective, and among the various dialysis modalities centre HD was the most cost-effective.[5]

The annual death for HD patients was 11.2% and cardiovascular disease remained the main cause of death accounting for 34% of all death. Infection has increased over the last four years and became the second most common cause of death in 2010, accounting for 24% of all deaths. Between 2001 and 2010, the annual prevalence of Hepatitis B in HD patients ranges from 4% to 6% while the prevalence of Hepatitis C continues to decline from 23% in 2001 to 7% in 2010.The cumulative risk of sero-conversion to Hepatitis B surface antigen (HBsAg) positive among sero-negative patients at entry into dialysis was 1.31% at seven years while for Hepatitis C virus (HCV) was 3.16%. It was reported that centres which still use manual dialyzer reprocessing systems run significantly higher risk of seroconversion.[4]

Chronic HD patients are uniquely vulnerable to the development of health-care associated infections because of multiple factors including exposure to invasive devices, immunosuppression, the lack of physical barriers between patients in the outpatient HD environment, and frequent contact with healthcare workers during procedures and care. Hence, efforts and actions designed to reduce the risk of infection are recommended for all setting where HD services are provided as advocated both by guidelines and the law.[6,7,8,9]

Haemodialysis is a method of removing waste products such as creatinine and urea, as well as free water from blood when the kidneys are in renal failure. The HD machine pumps the patient's blood and the dialysate through the dialyser. The dialyser is the piece of equipment that actually filters the blood. The dialyser may either be discarded after each treatment or be reused.[10]

Dialyser reuse has historically been practised in light of perceived potential benefits for the dialysis provider and the patient. The three major perceived advantages for the provider include: an economic benefit, the ability to use high-flux dialysers which traditionally have been more expensive, and a favourable environmental impact as a result of decreased generation of biomedical waste. From the patient's standpoint, the conventional argument for reprocessing of dialysers is to improve blood-membrane biocompatibility, particularly that of cellulose membranes, and the prevention of first-use syndromes usually associated with the use of ethylene oxide-sterilised dialysers.[11]

However, some of the original reasons are no longer valid. The availability of cheaper high-flux dialysers for single use means that the traditional benefit of the ability to reuse such dialysers no longer holds true. Synthetic membranes with improved blood membrane biocompatibility are now widely available and first-use syndromes have become less of an issue, particularly as ethylene oxide sterilisation is increasingly being replaced by other methods including gamma irradiation, steam, and most recently, electron beam sterilisation.[11] The cost of reprocessing and using reprocessed dialyser is not necessary cheaper due to the rise in the cost of several components required to implement dialyser reprocessing such as: the cost of staff overheads, utilities, chemicals (such as peracetic acid) and consumables, equipments (dialyser reprocessing machines, sterilant auto dilutor, dialyser auto rinser), additional physical space and facility (dedicated room for reprocessing with effective exhaust system, dialyser storage racks and clinical sinks).

In Malaysia, in 2010, 90% of patients undergoing haemodialysis were using reuse dialysers and 19% of patients used their dialysers for at least 13 times. About 80% of patients were using dialysers made from synthetic membrane. Currently, MOH haemodialysis units are using a fully automated dialyser reprocessing machine.[4] The Guideline on HD Quality and Standards by the Medical Development Division, Ministry of Health in 2012 states that HBsAg positive patients, HCV positive patients and Human Immunodeficiency Virus (HIV) positive patients shall be isolated in a separate room and shall be dialysed using separate machines, equipment and instruments. Single use dialyser is mandatory for Hepatitis B & C co-infection and HIV positive patients.[9]

The Centers for Disease Control and Prevention (CDC) in the United States of America (U.S.A.), in their Recommendations for Preventing Transmission of Infections among Chronic Haemodialysis Patients in 2001, states that dialysers should not be reused on HBsAg-positive patients because HBV is efficiently transmitted through occupational exposure to blood. Hence, reprocessing dialysers from HBsAg-positive patients might place HBV-susceptible staff members at increased risk for infection.[7]

The percentage of dialyser reuse varies according to countries. The proportion of dialysis centres that reuse dialysers in the U.S.A. was expected to decline to 40% of dialysis centres in 2005.[11] Japan, most of Middle East and a few scattered countries in Europe and South America do not practice any dialyser reuse.[12]

Reprocessing of disposable medical devices for single use as a cost saving measures has been debated, not only for dialysers, but also for sundry and other medical devices. In the case of dialyser reuse, the main concern has been the risk to life, but other issues have been raised such as risk for infection and pyrogenic reactions, toxicity from disinfectants (formaldehyde, glutaraldehyde, peracetic acid, sodium hypochlorite), reduced dialyser performance, impaired removal of large molecules, and the validity of the dialyser blood volume measurement as a criterion for assessing dialyzer function.[13,14,15]

Potential errors and breakdowns in the reuse process are continuing concerns. The risk may move beyond bacteria into the realm of viruses and prions.[15,16] In MOH haemodialysis units, due to shortage of staffs, the dialyser reprocessing procedures are now performed by medical attendants. They are technically at risk of exposure to blood borne infections if adherence to standard precautions is not observed. It has been claimed that single use dialyser decreases rates of infection and contamination, likelihood errors and accidents, and risks associated with exposure to germicides and denatured blood products. Single use simplifies some of the operational aspects of haemodialysis and is convenient. The risk for medicolegal liability is also negligible in single use dialyser compared with reuse dialyser.[11] Therefore, there is a need to reassess the dialyser reprocessing practice in MOH haemodialysis units. This health technology assessment (HTA) was requested by the Head of Nephrology Services, Ministry of Health, Malaysia.

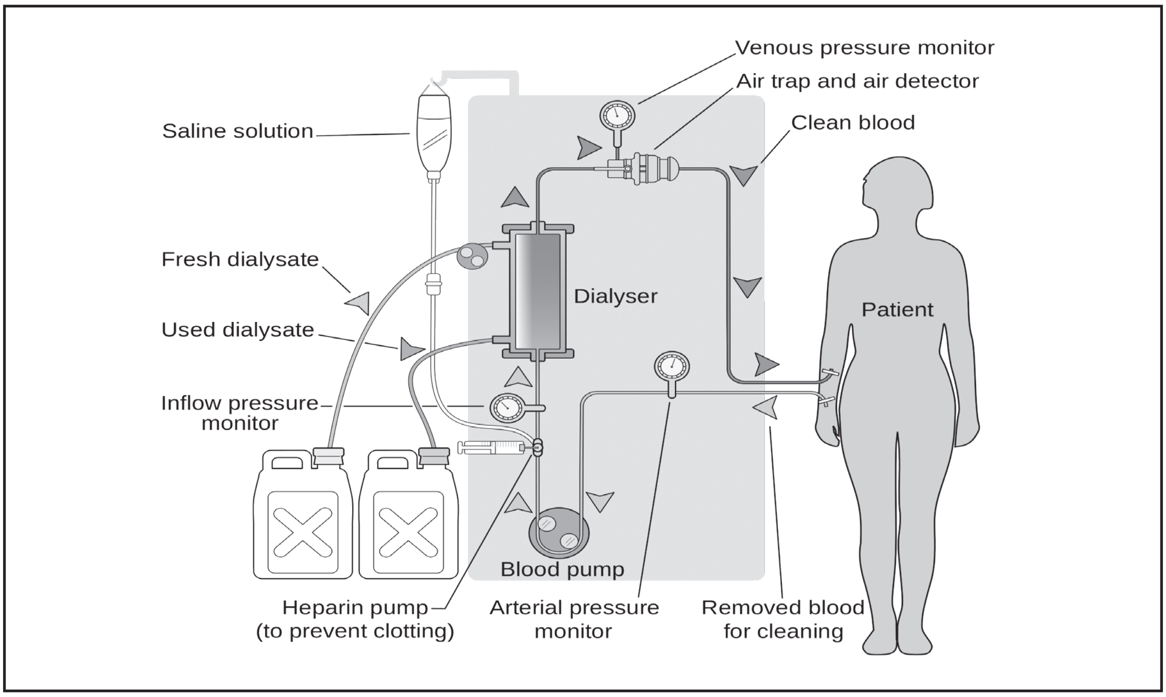
2 TECHNICAL FEATURES

2.1. Principles of haemodialysis

The primary goal of haemodialysis is to restore the intracellular and extracellular fluid environment that is characteristic of normal kidney function. This is accomplished by the transport of solutes such as urea from the blood into the dialysate and by the transport of solutes such as bicarbonate from the dialysate into the blood. Solute concentration and molecular weight are the primary determinants of diffusion rates. Small molecules such as urea diffuse quickly, whereas compartmentalised and larger molecules such as phosphate, β_2-microglobulin (β_2M) and albumin and protein-bound solutes (such as p-cresol), diffuse much more slowly. In addition to diffusion, solutes may pass through the pores in the membrane by means of a connective process driven by hydrostatic or osmotic pressure gradients - process called ultrafiltration. During ultrafiltration there is no change in solute concentration. Its primary purpose is the removal of excess total body water. For each dialysis session, the patient's physiological status should be assessed so that the dialysis prescription can be aligned with the goals for the session.[17]

During HD, blood is drawn out through a tube at a rate of 200-400 millilitre (mL)/min. The tube is connected to a needle inserted in the dialysis fistula or graft, or connected to one port of a dialysis (catheter) without needles. The blood is then pumped through the dialyzer, and then the processed blood is pumped back into the patient's bloodstream through another tube (connected to second needle or port) as shown in Fig. 1. The newest dialysis machines on the market are highly computerised and continuously monitor an array of safety-critical parameters including blood and dialysate flow rates, dialysis solution conductivity, temperature, pH, and analysis of the dialysate for evidence of blood leakage or presence of air.[10]

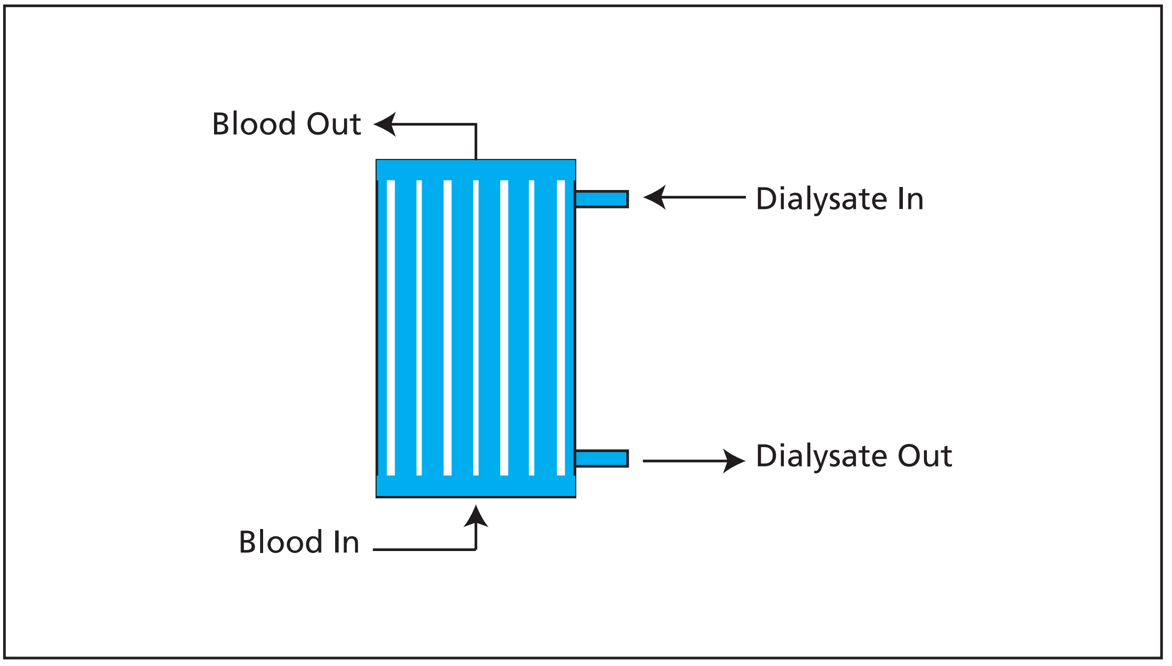
Figure 1. Schematic of a haemodialysis circuit



2.2. Dialyser

The heart of haemodialysis is the dialyser. Almost all dialysers in use today are of the hollow-fibre variety. The dialyser consists of bundle of semi-permeable hollow fibres (tubes) surrounded by a hard plastic casing (shell). The fibres are potted into the casing with an impermeable glue at either end. Fluid distribution caps are then glued into place. Blood can then flow into one fluid distribution cap along the interior of the fibre (tube-side) to the exit distribution cap, and thence out of the dialyser. Dialysate, basically distilled water with an electrolyte and pH composition similar to that of blood plasma flows counter-current to the blood on the outside of the fibres (shell-side).[18]

Figure 2. Schematic diagram of hemodialysis haemodialyser flow



Membrane and flux

Dialyser membranes come with different pore sizes. Those with smaller pore size are called "low-flux" and those with larger pore sizes are called "high-flux". Some larger molecules such as $β_2$M are not removed with low-flux dialysers. Lately, the trend has been to use high-flux dialysers. The goal of high-flux membranes is to pass relatively large molecules such as $β_2$M but not to pass albumin.[10,19]

Dialyser membranes used to be made primarily of cellulose (derived from cotton linter). The surfaces of such membranes are not very biocompatible because exposed hydroxyl groups would activate complement in the blood passing by the membrane. Therefore, the basic "unsubstituted" cellulose membrane was modified. One change was to cover these hydroxyl groups with acetate groups (cellulose acetate), and another was to mix in some compounds that would inhibit complement activation at the membrane surface (modified cellulose). The original "unsubstituted cellulose" membranes are no longer in wide use, whereas, cellulose acetate and modified cellulose dialysers are still used. Cellulosic membranes can be made in either low-flux or high-flux configuration, depending on their pore size.[10]

Another group of membranes is made of synthetic materials using polymers such as polyarylethersulfone, polyamide, polysulfone, polyvinylpyrrolidone, polycarbonate, polymethymethacrylate and polyacrylonitrile. These synthetic membranes activate complement to a lesser degree than unsubstituted cellulose membranes. Synthetic membranes can be made of either low-or-high flux configuration but most are high-flux. Nanotechnology is being used in some of the most recent high-flux membranes to create a uniform pore size.[10,19]

Dialyser size and efficiency

Dialysers come in many different sizes. A larger dialyser with a larger membrane area (A) will usually remove more solutes than a smaller dialyser especially at high blood flow rates. This also depends on the membrane permeability coefficient (K_0) for the solute in question. So dialyser efficiency is usually expressed as the (K_0A) - the product of permeability and area. Most dialysers have membrane surface areas of 0.8 to 2.2 square metres, and values of K_0A ranging from about 500 to 1500 mL/min.[10]

Single use dialyser

The dialyser may either be discarded after each treatment or be reused. Single use dialysers are initiated just once and discarded.[10]

Reuse dialyser

Dialyser reuse or reprocessing can be defined as the disinfection of a dialyser for multiple uses for the same patient.[12]

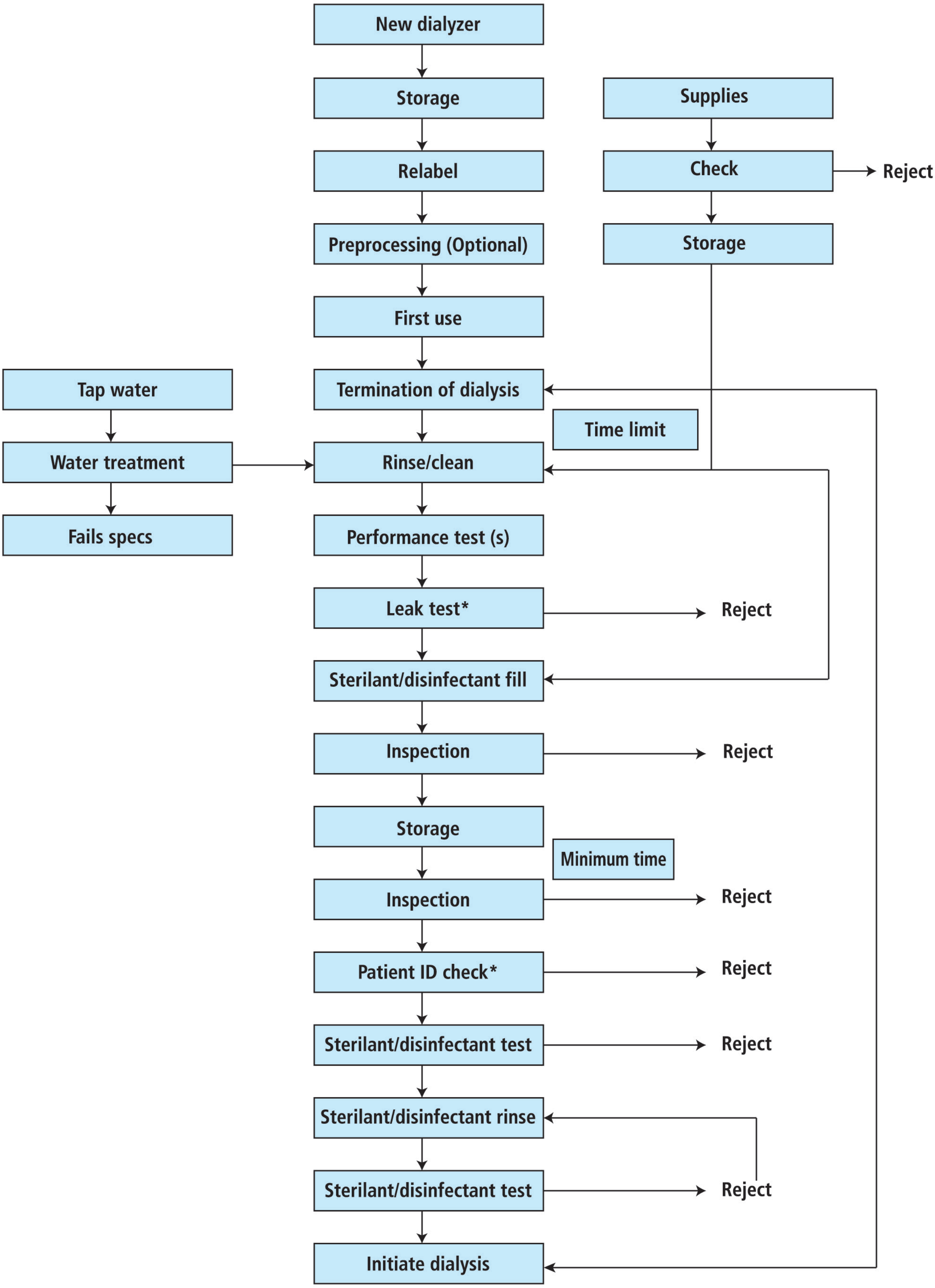
The practice of reusing dialysers has been performed in the U.S.A. since the 1960s. Until mid-1990s, even dialysers labelled by manufacturers for single use were reused. In light of widespread practice of reuse and its potential effect on patient care, the U.S. Food and Drug Administration (FDA) determined that manufacturers' labelling must reflect the actual commercial marketing and clinical use of haemodialysers. Labelling requirements for multiple-use dialysers are covered in the FDA's "Guidance for Haemodialyser Reuse Labelling", 6 October 1995. Dialysers labelled for multiple use must include instructions for their safe and effective reuse.[20]

There are two ways of reusing dialysers. There is manual reuse, which involves the cleaning of the used dialyser by hand. The dialyser is semi-disassembled then flushed repeatedly before being rinsed with water. It is then stored in a liquid disinfectant until its next use. The second is the automated reuse by means of a medical device The dialyser is automatically cleaned by machine and then filled with liquid disinfectant for storage.[10] A majority of facilities that reprocess dialysers are now using a peracetic acid mixture as the primary reuse reagent.[15,21] The peracetic acid mixture components include hydrogen peroxide, acetic acid and peroxyacetic acid.[15] The other reuse reagents include formaldehyde, glutaraldehyde and sodium hypochlorite. In the U.S.A. in centres practising reuse, the use of formaldehyde declined from 100% in 1976 to 20% in 2002. The use of glutaraldenyde declined from 8% in 1990 to 4% in 2002, while the use of peracetic acid increased from 5% in 1983 to 72% in 2002.[14,15,21]

According to the Association for the Advancement of Medical Instrumentation (AAMI) Standards for reuse of dialysers, the multiple use of a dialyser begins with the labelling of the new dialyser and then continues with the reprocessing procedures which involve many steps as shown in Figure 3 below.[20] The Guideline on HD Quality and Standards by the Medical Development Division, Ministry of Health in 2012, states that dialysers with [Total Cell Volume (TCV) also describes as fibre bundle volume, or blood compartment volume] of <80% or failed the leak test with TCV <80% shall not be reused.[9]

SYSTEMS DIAGRAM FOR REPROCESSING DIALYZERS

Figure 3. Systems diagram for reprocessing dialyzers



*This step may be done later but shall precede initiation of dialysis.

3 POLICY QUESTION

In MOH haemodialysis units, should single use dialyser be used for all haemodialysis patients or only for those with infectious diseases such as Hepatitis B, Hepatitis C, Hepatitis B & C co-infection or HIV infection?

4 OBJECTIVES

4.1. To assess the safety, effectiveness, economic implications, organizational, legal or environmental impacts of single use dialyser compared with reuse dialyser for haemodialysis of patients with end stage renal disease (ESRD) through a systematic review of the literature. (**Part A**)

4.2. To assess the cost-effectiveness of single use dialyser compared with reuse dialyser for haemodialysis of patients with ESRD in Malaysian public hospitals by conducting a local economic evaluation. (**Part B**)

The following research questions were addressed:-

- How safe is single use dialyser compared with reuse dialyser?
- What are the short and long term benefits of using single use dialyser compared with reuse dialyser for haemodialysis of patients with ESRD?
- What is the economic implication of using single use dialyser compared with reuse dialyser?
- What are the organizational, legal or environmental impacts of single use dialyser compared with reuse dialyser?
- What is the economic implication of using single use dialyser compared with reuse dialyser for haemodialysis patients with ESRD in Malaysia hospital (public hospital)?

5 METHODS

5.1. PART A (SYSTEMATIC REVIEW OF LITERATURE)

5.1.1. Literature search strategy

Studies were identified by searching electronic databases. The following databases were searched through the Ovid interface: MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, EBM Reviews-Cochrane Database of Systematic Reviews (2005 to January 2013), EBM Reviews-Cochrane Central Register of Controlled Trials (January 2013), EBM Reviews – Database of Abstracts of Review of Effects (1st Quarter 2013), EBM Reviews-Health Technology Assessment (1st Quarter 2013), EBM Reviews-NHS Economic Evaluation Database (1st Quarter 2013), EMBASE 1988 to 2013 Week 09. Parallel searches were run in PubMed. Appendix 3 showed the detailed search strategies. No limits were applied to the search. The last search was run on 14 February 2013. Additional articles were identified from reviewing the references of retrieved articles. General search engine was used to get additional web-based information.

5.1.2. Study Selection

Based on the policy question the following inclusion and exclusion criteria were used:-

5.1.3. Inclusion criteria

- Study design: HTA report, Systematic Review (SR), Randomised Controlled Trial (RCT), Non Randomised Controlled Trial, Cohort, Case control studies, Pre and post intervention studies, Cross sectional studies, case series, and studies which include economic evaluation.
- Population: Patients with end stage renal disease on haemodialysis (adult and children).
- Intervention: Single use dialyser.
- Comparators: Reuse dialyser or reprocessed dialyser.
- Outcome:
  - i. Adverse events or complications associated with single use dialyser or reuse dialyser : [infection, pyrogenic reactions (characterised by chills, fever, rigors, and sometimes hypotension in patients who were afebrile before dialysis treatment), allergic reactions, first-use reactions or syndromes (characterised by nausea, malaise, weakness, a sensation of burning or heat throughout the body, profuse perspiration, respiratory distress, hypotension and cardiopulmonary arrest)]
  - ii. Changes in membrane integrity
  - iii. Mortality risk
  - iv. Survival rate
  - v. Hospitalisation
  - vi. Economic (Cost–effectiveness, cost-analysis)
  - vii. Organizational
  - viii. Legal implication
  - ix. Environmental
- Full text articles published in English.

5.1.4. Exclusion criteria:-

- Study design: Animal study, laboratory study, narrative review
- Non English full text article.

Based on the above inclusion and exclusion criteria, study selection were carried out independently by two reviewers. The titles and abstracts of all studies were assessed for the above eligibility criteria. If it was absolutely clear from the title and / or abstract that the study was not relevant, it was excluded. If it was unclear from the title and / or the abstract, the full text article was retrieved. Two reviewers assessed the content of the full text articles. Disagreement was resolved by discussion.

5.1.5. Quality assessment strategy

The methodological quality of all the relevant full text articles retrieved was assessed using the Critical Appraisal Skills Programme (CASP) tool by two reviewers.[22] For SR the criteria assessed include selection of studies, assessment of quality of included studies, heterogeneity of included studies. For RCT, the criteria assessed were randomisation, allocation concealment, blinding, explanation on loss to follow-up, and intention to treat analysis. For cohort study, the criteria assessed were selection of the cohort, accurate measurement of exposure and outcome, confounding factors, follow-up adequacy and length. For case control study, the criteria assessed were selection of the cases and control, accurate measurement of exposure, blinding and confounding factors. For economic evaluation, the criteria assessed include comprehensive description of competing alternatives, effectiveness established, effects of intervention identified, measured and valued appropriately, relevant resources and health outcome costs identified, measured in appropriate units and valued credibly, discounting, incremental analysis of the consequences and costs of alternative performed and sensitivity analysis performed. The CASP checklist is as in Appendix 4. All full text articles were graded based on guidelines from the U.S./Canadian Preventive Services Task Force (Appendix 1).[23]

5.1.6. Data extraction strategy

Data were extracted from included studies by a reviewer using a pre-designed data extraction form (evidence table as shown in Appendix 5) and checked by another reviewer. Disagreements were resolved by discussion. Details on:(1) methods including study design, (2) study population characteristics including gender, age, (3) type of intervention, (4) comparators, (5) type of outcome measures including: a) adverse events or complications related to the use of single use dialyser or reuse dialyser such as infection, pyrogenic reactions, allergic reactions, first-use reactions or syndromes, b) changes in membrane integrity, c) mortality risk, d) survival rate, e) hospitalisation, f) economic evaluation, f) organizational, g) legal implication, and h) environmental impact were extracted. The extracted data were presented and discussed with the expert committee.

5.1.7. Methods of data synthesis

Data on the safety, efficacy and cost implication of using single use dialyser compared to reuse dialyser were presented in tabulated format with narrative summaries. No meta-analysis was conducted for this review.

5.2. PART B (LOCAL ECONOMIC EVALUATION)

5.2.1. This economic evaluation was designed from provider (Ministry of Health) perspective based on haemodialysis unit in general public hospital.

5.2.2. Model Structure

The evaluation was conducted using Markov cohort analysis where the average five years' costs and consequences (quality adjusted life years, QALY) for the patient who received either type of dialyser were evaluated. The model structure was simplified from a published Canadian model whereby patient who received single use/reuse dialyser progress to either requiring transplant, or remaining in the dialysis state, or died within 1 year cycle (Figure 1).[1] The cost and benefit was discounted at 3%.

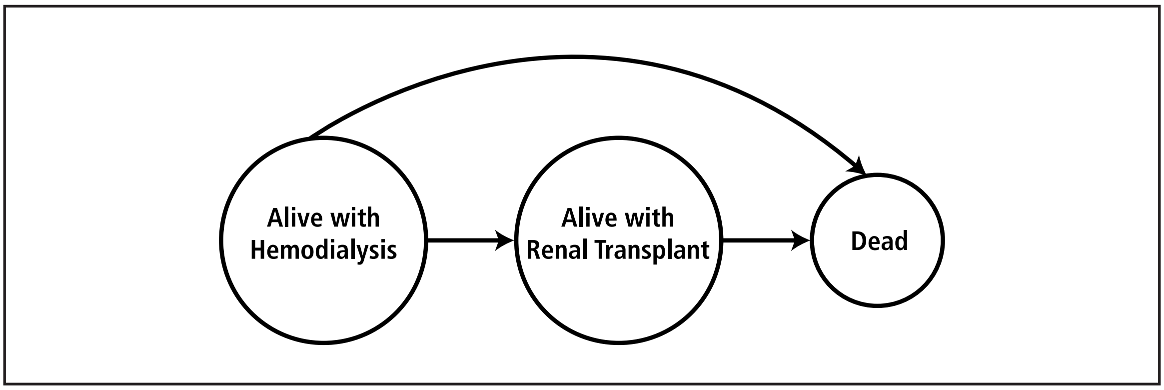


Figure 1: Markov state diagram for dialysis patient progression between three health states

5.2.3. Model Input

Model inputs were summarised in Table 1. Cost considered includes cost for outpatient, hospitalisation, renal transplant, and dialysis. All costs were obtained from local data source. The cost for haemodialyser was based on micro-costing of high flux dialyser that include the cost of biohazardous waste disposal, filter, personnel, test strip (assuming 20 dialyser processed per day), equipment (assuming 10 years useful life).[2] It was assumed based on the national pattern, that patient need three haemodialysis sessions per week.[3] Cost of renal transplant was obtained from micro-costing of resource used for renal transplantation from dead donor, which made up 60% of transplant cases in Malaysia.[3,4]

Table 1: Parameter input in the model

VARIABLE		RANGE	SOURCE
Cost of synthetic haemodialyser per run	MYR 52.10		2
Cost of peracetic acid reuse per run	MYR 9.30		2
Yearly cost of outpatient dialysis per patient	MYR 2,125.26		7
Yearly cost of hospitalisation per haemodialysis patient treated with synthetic single-use dialysis	MYR 279.72		7
Yearly cost of transplantation			
Year 1	MYR 95,012.86		4
Years 2 and on	MYR 49,461.93		4
Annual mortality risk HD single use	0.152	0.145 - 0.159	1
Annual number of hospital days HD single use	7.4	4.2 - 10.7	1
Average utility score for in-centre HD pt	0.43	0.35 - 0.51	1
Average utility score for renal transplant pt	0.84	0.79 - 0.89	1
Annual rate of transplantation	0.0835		1
Annual mortality risk for transplant patients	0.045		1
RR mortality reuse versus single use	1.01	0.996 - 1.027	1
RR hospitalisation reuse versus single use	1.1	1.06 - 1.15	1
Adj hospitalisation rate reuse	2.25/year		5
Adj hospitalisation rate single	2.19		5

There was no local utility estimate available. Hence, utility, and baseline epidemiology risk were obtained from secondary Canadian data.[1] The hospitalisation rate for single and reuse dialyser was based on estimate from published US cohort.[5]

5.2.4. Economic Evaluation

If the intervention group are more expensive and effective than usual care group, then incremental cost-effectiveness ratio (ICER) will be calculated as the difference between the cost for each group divided by the difference in effectiveness. The threshold of MYR 32,000 was used to determine the cost-effectiveness of the intervention at baseline.[6]

5.2.5. Sensitivity Analysis

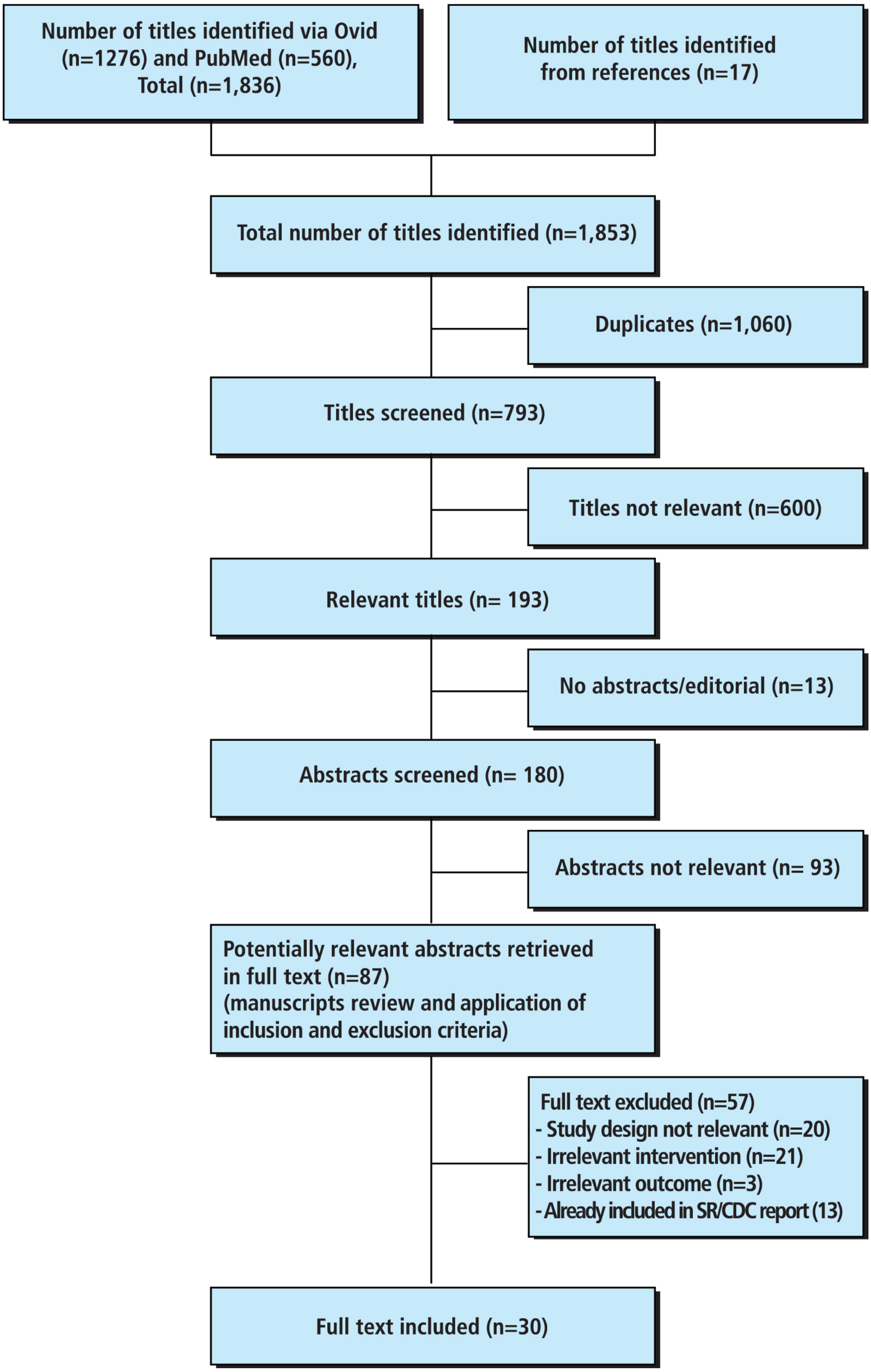
Simple one-way sensitivity analysis was conducted on the following parameters: cost of single use dialyser, relative risk of mortality and hospitalisation for reuse, probability of transplant, cost of transplant, discount rate. This was done by varying each of these uncertain components individually, while the others retain their base-case specification, in order to establish the separate effect of each component on the results of the analysis. The variation was chosen arbitrarily at 50% of the baseline value, though cost of reuse dialyser was varied from MYR 0-MYR 1,0000 in order to investigate possibilities of reuse dialyser to be more expensive than single use dialyser. Probabilistic sensitivity analysis was also conducted by assigning a distribution to appropriate parameters in the model. Each time the model is run, the model will randomly 'select' one value for each parameter, record the results and present the variation in results. Threshold analysis was also conducted to determine the breakeven point, where the expected values are equal for both reuse and single use dialyser.

6 RESULTS

6.1. PART A (SYSTEMATIC REVIEW OF LITERATURE)

A total of 1,836 titles were identified through the Ovid interface: MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, EBM Reviews-Cochrane Database of Systematic Reviews (2005 to January 2013), EBM Reviews-Cochrane Central Register of Controlled Trials (January 2013), EBM Reviews – Database of Abstracts of Review of Effects (1st Quarter 2013), EBM Reviews-Health Technology Assessment (1st Quarter 2013), EBM Reviews-NHS Economic Evaluation Database (1st Quarter 2013), EMBASE 1988 to 2013 Week 09 and PubMed. Seventeen titles were identified from references of retrieved articles. After removal of 1,060 duplicates, 793 titles were screened. A total of 193 titles were found to be potentially relevant and 180 abstracts were screened using the inclusion and exclusion criteria. Of these, 93 abstracts were found to be irrelevant. Eighty seven potentially relevant abstracts were retrieved in full text. After reading, appraising and applying the inclusion and exclusion criteria to the 87 full text articles, 30 full text articles were included and 57 full text articles were excluded. The articles were excluded due to irrelevant study design (n=20), irrelevant intervention (n=21), irrelevant outcome (n=3) and already included in a systematic review / CDC report (n=13). The excluded articles are listed in Appendix 6. The 30 full text articles finally selected for this review comprised of one SR, two RCTs, three cross over design, five cohort studies, one pre and post-intervention study, 11 cross sectional studies, three case series, one cost-utility analysis, two cost analysis and one cost minimisation analysis. There was no HTA report on single use dialyser versus reuse dialyser retrieved.

FLOW CHART OF STUDY SELECTION



6.1.1. SAFETY OF SINGLE USE DIALYSER VERSUS REUSE DIALYSER

Fifteen articles related to the safety of single use dialyser versus reuse dialyser were included in this review: one RCT, one cross over design with random order to allocation, two cohort studies, one pre and post intervention study, seven cross sectional studies and three case series. The articles were published between 1981 and 2000. Most of the studies were conducted in the U.S.A. (80%), and the rest of the studies were conducted in Canada, Belgium and Portugal (one each).

Risk of bias

The RCT and the cohort studies included have unclear risk of bias whereby for the RCT the method of randomisation (sequence generation) and allocation concealment was unclear. As for the two cohort studies, none mentioned about blinding. The cross sectional studies and case series have potentially high risk of bias. The results are summarised in Table 1.

Table 1. Assessment of risk of bias of included studies

Study Design (RCT) Criteria assessed Study	**Randomisation (sequence generation)**	**Allocation concealment**	**Blinding**	**Intention to treat analysis**	**Explanation Loss to follow-up**
Pereira et al.[25]	Can't tell (method of randomisation not mentioned)	Can't tell	Yes	Yes	Yes
Study Design (Cohort) Criteria assessed Study	**Selection**	**Exposure accurately measured**	**Outcome accurately measured**	**Confounding factors**	**Follow-up of subjects**
Powe et al.[26]	Yes	Yes	Can't tell	Yes	Yes
Pegues et al.[35]	Yes	Yes	Can't tell	Can't tell	Yes

a. Bacterial infection and pyrogenic reactions

Infection is a major cause of morbidity and mortality in patients on chronic haemodialysis. In addition to bacteraemia, gram-negative organisms can cause pyrogenic reactions by producing endotoxins.

From January 1980 through June 1999, the CDC investigated 16 outbreaks of bacteraemia or pyrogenic reactions in haemodialysis patients. Of these, inadequate dialyser reuse practices were implicated in eight outbreaks as shown in Table 2. Other causes of outbreaks were related to inadequate water treatment, contaminated dialysis fluid, contaminated dialysis machine and infected central vein catheters.[24 level II-3] Similarly, in Belgium, a small cluster of waterborne septicaemia with *Pseudomonas species* occurred in three patients in a dialysis unit despite regular control of bacterial contents of tap water and dialysate conforming to preset standards. The cluster occurred only in patients treated with formaldehyde reused dialysers.[25 level II-3]

Table 2. Outbreaks of bacterial infection and / or pyrogenic reactions associated with reuse of dialyser.

Study (Country)	Description of outbreak	Cause of outbreak
Roth VR, Jarvis WR. (U.S.A.)	• (*Mycobacterium chelonae*) in 27 patients from one haemodialysis centre in 1982	• Inadequate concentration of dialyser disinfectant (2% formaldehyde)
	• Systemic non tuberculous *mycobacterial* infections in five high-flux dialysis patients; two deaths	• Inadequate concentration of dialyser disinfectant (2.5% Renalin), inadequate disinfection of water treatment system
	• Gram-negative Bacteraemia and pyrogenic reactions in six patients	• Dialyser disinfectant diluted to improper concentration (2.5% Renalin)
	• Gram-negative Bacteraemia in six patient	• Dialyser disinfectant diluted to improper concentration, water for reuse did not meet Advancement of Medical Instrumentation (AAMI) standards
	• Nine pyrogenic reactions and five gram-negative bacteraemia in 11 patients	• Inadequate mixing of dialyser disinfectant (Renalin)
	• Gram-negative bacteraemia in 33 patients in six haemodialysis centres	• Dialyser disinfectant (chlorine dioxide-based disinfectant) altered the dialyser membrane integrity causing leaks in the membrane
	• Bacteraemia in six patients (*Klebsiella pneumonia)* in 1992: all blood isolates had similar plasmid profiles	• Dialyser contaminated during removal and cleaning of headers with gauze, staff not routinely changing gloves; dialysers not processed for several hours after disassembly and cleaning
	• Pyrogenic reactions in three high-flux dialysis patients	• Dialyser reprocessed with two disinfectants (4% formaldehyde and 2.5% Renalin) was taught to impair membrane integrity, water for reuse did not meet AAMI standards
Vanholder R, Vanhaecke E, Ringoir S. (Belgium)	• *Pseodomonas aeruginosa*, *P. Maltophilia*, and / or *P. Vesicularis* were found in the blood cultures of three patients in whom four pyrogenic reactions developed	• *Pesudomonas* were cultured from the effluent of two dialysers reprocessed with formaldehyde and not yet use, these two dialysers had extremely low formaldehyde concentrations. The problem appeared to be related to the inadequate mixing of the sterilant with the tap water used in the automated reprocessing device.

Powe et al. conducted a longitudinal cohort study with seven years of follow-up among 4,005 haemodialysis patients with ESRD to identify the risk factors for septicaemia among them. The study found that older patients (age > 65 years), and patients with diabetes were at an increased risk of septicaemia: the Adjusted Risk Ratio = 1.75; 95% Confidence Interval (CI): 1.48 to 2.06, and 1.26; 95% CI: 1.06 to 1.50, respectively. Patients who reused dialysers had a 28% higher risk of septicaemia than patients who did not reuse dialysers over the entire follow-up period: Adjusted Risk Ratio = 1.28; 95% CI: 1.05 to 1.56. They also reported that haemodialysis patients who experienced an episode of hospital-managed septicaemia had more than a twofold higher risk of death from any cause: Adjusted Risk Ratio = 2.40; 95% CI: 2.12 to 2.72 and had a ninefold greater risk of death from septicaemia: Adjusted Risk Ratio = 9.79; 95% CI: 6.49 to 14.76.[26 level II-2]

Based on the National Surveillance of Dialysis Associated Diseases in the U.S.A. which was conducted by the CDC in collaboration with Health care Financing Administration in 1992, 1994 and 1995, Tokars et al. reported that reuse of dialysers, used of high flux dialyser membranes and used of high flux dialysis were associated with significant increased reporting of pyrogenic reactions in the absence of septicaemia.[27-29 level II-3]

b. Viral infection

Viruses such as HBV, HCV and HIV pose potential infection risk to employees and patients in haemodialysis centres. Tokars et al. reported that reuse of dialysers was not associated with increased risk of HBV infection in either patients or staffs (data not shown).[27-30 level II-3] Similarly, an earlier study by Favero et al. reported that there was no increased in the incidence of hepatitis B among patients or staff members associated with long-term haemodialysis centres that practiced multiple use as compared with those centres that practiced single use of dialyser. Of 6,079 patients, 166 (2.7%) became hepatitis HBsAg positive in 96 centres practicing reuse, whereas 495 of 18,947 (2.6%) became HBsAg positive in 439 centres practicing single use. Among staff members, 75 of 3,049 (2.5%) became hepatitis HBsAg positive in centres practicing reuse versus 200/8,696 (2.3%) in centres practicing single use. Nearly 95% staff members who became HBsAg-positive were associated with centres having at least one HBsAg-positive patient.[31 level II-3]

According to the CDC, from April through August 1994, outbreaks of HBV infection occurred in five chronic haemodialysis centres in California, Nebraska, and Texas. These outbreaks were investigated by the state and local public health officials and the CDC. Cases of acute HBV infection were identified through routine serology screening in 0.7% to 70% of susceptible patients at the five centres. Transmission of HBV from haemodialysis patients with chronic HBV infection to susceptible patients resulted from failure to identify and isolate HBV-infected patients during haemodialysis, sharing of staff, equipment, and supplies among patients, and failure to vaccinate susceptible patients against hepatitis B.[32 level II-3]

Tokars et al. reported that Anti-HCV prevalence among patients and staffs was similar between centres that reuse and centres that did not reuse dialysers.[27-30 level II-3] In 1992, the anti-HCV prevalence among patients was (reuse = 8.1%; no reuse = 8.3%, P = 0.6) and among staffs (reuse = 1.6%; no reuse = 1.5%, P = 0.9).[27 II-3] In 1997, the anti-HCV prevalence among patients was (reuse = 9.3%; no reuse = 9.3%) and among staffs (reuse = 1.6%; no reuse = 1.7%, P=0.9).[30 II-3] Similarly, in Portugal Pinto dos Santos et al. reported that the incidence of HCV infection in patients treated in units that reprocessed dialysers (6.1%) was not significantly different from that among patients treated in units that did (7.4%).[33 level II-3]

According to National Surveillance of Dialysis-associated Diseases in the United States, in 1997, there was no report of nosocomial HIV transmission in dialysis centres.[30 level II-3]

c. New Dialyser Syndrome (First-Use Syndrome)

Since 1982, the FDA has been monitoring report concerning severe hypersensitivity reactions with new dialysers (also called first-use syndrome) that occur in ESRD patients. These anaphylactic-like reactions occur within the first few minutes of dialysis treatment.

In the U.S.A. based on the National Surveillance of Dialysis Associated Diseases, new dialyser syndrome was reported in patients at 24% of dialysis centres in 1992 and 28% of dialysis centres in 1994 which showed a reduction from 43% of dialysis centres in 1984. The proportion of centres reporting new dialyser syndrome varied by type of dialyser membrane used, and was higher among centres reusing dialysers: Odds Ratio (OR) = 1.6, $P < 0.001$ in 1992, and OR = 1.5, $P = 0.0009$ in 1994. Logistic regression model confirmed that the new dialyser syndrome was reported most frequently by centres using regenerated cellulose and cuprophan membranes. In 1992, the OR was 2.5, $P < 0.001$ for regenerated cellulose, and OR = 2.2, $P < 0.001$ for cuprophan. In 1994, the OR was 1.5, $P = 0.001$ and OR = 1.9, $P < 0.001$ for regenerated cellulose and cuprophan, respectively.[27-28 level II-3]

Key J, Nahmias M, Acchiardo S reported a series of hypersensitivity reaction on first-time exposure to cuprophan hollow fibre dialyser among three of 45 patients in the U.S.A. who have been maintained on haemodialysis using a regenerated cellulose hollow fibre artificial kidney (HFAK) and were dialysed on cuprophan HEAK for the first time. Within seconds in one patient, and within 10 to16 minutes in two patients, respiratory distress, urticaria, pruritus, hypertension / hypotension, and facial oedema developed. They were treated with oxygen, epinephrine, and diphenhydramine. Two patients received an intermittent positive pressure breathing treatments and one received intravenous methyl-prednisolone. After allowing 10 to15 minutes for stabilisation, the dialysis was resumed on a non-cuprophan hollow fibre artificial kidney (regenerated cellulose hollow fibre dialyser). Patients were discharged with no sequelae. The cause of the hypersensitivity reaction is unknown.[34 level II-3]

d. Anaphylactoid Reactions with Reuse Dialysers

Pegues et al. reported an outbreak of anaphylactoid reactions associated with reuse of hollow fibre haemodialysers at a haemodialysis centre in Virginia, U.S.A. From July 18 through November 27, 1989, 12 anaphylactoid reactions occurred in 10 patients: one patient required hospitalisation, no patients died. Anaphylactoid reactions occurred within minutes of initiating dialysis and were characterised by peripheral numbness and tingling, laryngeal oedema or angiooedema, facial or generalised sensation of warmth, and / or nausea or vomiting. All 12 anaphylactoid reactions occurred with dialysers that have been reprocessed with an automated reprocessing system. Conventional hollow fibre dialysers with cellulose acetate or cuprophan membrane and high flux polysulfone hollow-fibre dialysers were used. The germicide used was Renalin 3.3%. A cohort study conducted by CDC, FDA and Virginia State Department of Health showed that the patients who experienced anaphylactoid reactions were significantly more likely than noncase-patients to be receiving angiotensin-converting-enzyme (ACE) inhibitors [7/10 versus 3/33; Relative Risk (RR) = 7.9; 95% CI: 2.5 to 25.2] and to have been exposed to reused dialysers rather than new dialysers (12/70 sessions versus 0/31 sessions: RR undefined; $P = 0.016$). In those sessions using a reused dialyser, the mean number of uses in case-sessions was significantly higher than in noncase-sessions (10.3 versus 6.2; $P = 0.016$). After reuse of dialysers was discontinued at the centre, no further anaphylactoid reactions occurred, despite continued administration of ACE inhibitors. The authors hypothesise that the interaction between dialyser that has been repeatedly reprocessed and reused, blood and additional factors, such as ACE inhibitors, increased the risk of developing anaphylactoid reactions.[35 level II-2]

e. Intradialytic symptoms

Pereira et al. conducted a RCT at the outpatient dialysis unit at St. Elizabeth's Medical Centre, Boston to compare the intradialytic signs and symptoms in patients dialysed with new or reprocessed cellulose membrane. The study involved 39 patients randomly assigned to 12 weeks dialysis with either new cellulose dialysers or reprocessed cellulose dialysers. Dialysers were processed with sodium hypochlorite (<1%) and disinfected with gluteraldehyde (0.8%) using an automated system. They found that during the 12 week study, none of the patients in either arm of the study experienced chills, rigors, or fever, and there was no differences in the number of episodes of symptomatic hypotension in patients on single use dialysers (8 ± 2) compared with patients on reuse dialysers (11 ± 3), P = 0.75.[36 level II-2] Similarly, a multiple crossover study with random allocation to order of treatment (single use dialyser or reuse dialyser) involving 51 patients at St Joseph's Hospital, Hamilton, Ontario, Canada using hollow fibre dialyser (cuprophane or cellulose acetate) conducted by Churchill et al. reported that there was no significant difference for temperature change during dialysis between single use dialyser and reuse dialyser (mean difference = 0.008°C). There were no differences for symptoms of pruritis, cramps, nausea, headache, chest pain, backache or fatique between single use and reuse dialysers.[37 level II-2]

In contrast, sub-analysis in 27 patients dialysed at the unit practicing reuse in the free standing dialysis centre (DCC) for a period of 334 patient months and were dialysed previously in a unit that did not practice reuse (University of Cincinnati Medical Centre) for a comparable earlier period totalling 321 months by Kant et al. found that most findings that might be associated with infection (fever, sweating, respiratory distress, chest pain, tenderness over fistula / graft) occurred significantly less frequent during the period in which dialysers were reuse. Hypotension, nausea and vomiting occurred significantly less frequent (P < 0.001) in dialysis unit practising reuse and cramps occurred with equal frequency in the two units.[38 level II-3]

f. Hazards due to reuse reagents

There was no retrievable evidence on the cumulative and long-term effects of chronic, low-dose exposure to reuse reagents (formaldehyde, hydrogen peroxide, sodium hypochlorite, glutaraldehyde and peracetic acid).

6.1.2. CHANGES IN MEMBRANE INTEGRITY

Another concern regarding reprocessed dialysers is maintenance of adequate solute clearance.

Seven articles related to changes in membrane integrity with reuse dialysers were included in the review: one RCT, two cross over design and four cross sectional studies. The articles were published between 1991 and 2000. Two of the studies were conducted multi centres and has large number of patients. The other five studies involved small number of patients ranged between five to 59 patients. The studies were conducted in the U.S.A., France, Brazil, and Australia.

Risk of bias

The RCT included has unclear risk of bias whereby blinding, intention to treat analysis and explanation of loss to follow-up was unclear. The cross sectional studies have potentially high risk of bias.

a. Clearances of Small Molecular Weight Solutes

Cheung et al. analyses data extracted from a randomised multicentre clinical trial (the HEMO Study) sponsored by the U.S. National Institutes of Health which involved 15 clinical centres with more than 45 dialysis units and examined the effects of reuse on urea and β_2M clearance by low-flux and high-flux dialysers reprocessed with various germicides. The most common high-flux dialysers used were CT190 (cellulose triacetate membrane) and F80 series (polysulfone membrane). The most common low-flux dialysers used were the CA series (CA170 and CA210; cellulose acetate membrane) and F8 (polysulfone membrane). The germicide used were peroxyacetic acid/acetic acid/hydrogen peroxide combination (Renalin)), bleach in conjunction with formaldehyde, gluteraldehyde or Renalin, and heated citric acid. The maximum number of times that a dialyser could be reused in the HEMO Study was originally set at 20 times. They reported that urea clearance by high-flux dialysers decreased by 1.9 ± 0.3% per 10 reuses, P < 0.001 with no significant differences among various types of dialysers and reprocessing methods, P = 0.096. Urea clearances by low-flux dialysers also deteriorated with reuse by (-1.00 ± 0.3%) per 10 reuses, P < 0.001, but the decrease was slightly lower than that of high-flux dialysers, P = 0.015 for all low-flux dialysers combined versus all high-flux dialysers combined. There was no significant differences in decreases of urea clearances between Renalin (-1.1 ± 0.4% per 10 reuses) and bleach-containing methods (-1.2 ± 0.4% per 10 reuses) for low-flux dialysers.[39 level II-1]

Leypoldt et al. in a crossover study involving six patients evaluated the effect of extensive reprocessing using Renalin on small and large solute clearances measured directly across the dialyser for two types of commonly used low-flux and two types of commonly used high-flux dialysers during use number 1, 2, 5, and 15. The Low-flux dialysers used were (TAF175 containing cuprammonium membrane and CA210 containing cellulose acetate membrane), and the high-flux dialysers used were (CT190G containing cellulose triacetate membrane and F80A containing polysulfone membrane). They found that urea, creatinine and phosphate clearances were generally slightly greater for high-flux than for low-flux dialysers. There was a trend for urea, creatinine and phosphate clearances to decrease with reuse for both low-flux and high-flux dialysers, but these differences were not statistically significant.[40 level II-3]

Kerr et al. studied the effect of prolonged use (up to 20 uses) of high-flux polysulfone dialysers reprocessed using peroxyacetic acid with or without bleach on the efficacy of removal of a range of molecular size solutes in 24 patients in hemodiafiltration unit over a two year period in France. They reported that for urea and creatinine, there were no significant differences in the percent reduction of these molecules for up to 20 uses: urea [(68.9 ± 1.1%) during first use and (66.3 ± 2.4%) during twentieth uses], creatinine [(63.9 ± 1.3) during first use and (64.9 ± 2.7%) during twentieth uses].[41 level II-3]

Quseph et al. reported two studies which evaluated the effect of reprocessing with peracetic acid / hydrogen peroxide on the performance of dialysers containing high-flux cellulose and polysulfone membranes. In the first study, eight men were treated with AM-UP-75WET dialyser. The dialyser contains 1.5 m^2 of regenerated cellulose membrane sterilised by gamma-irradiation. Removal of urea and β_2M were determined during treatments 1, 4, and 12. In the second study, nine patients were treated with F80B dialyser which contains 1.8 m^2 of polysulfone membrane and is sterilised with ethylene oxide. Removal of urea and β_2M were determined during treatments 1, 5, 10, and 15. The studies found that blood compartment volumes of the AM-UP-75WET dialysers remained greater than 80% of the initial value after 12 treatments in all eight patients. Blood compartment volumes of F80B dialysers remained greater than 80% of the initial value for all nine patients. However, the volume of four of these dialysers subsequently decreased to 80% of the initial value, so that only five dialysers completed 15 treatments. Urea removal, expressed as Kt/V, did not change with reuse for either dialysers. For AM-UP-75WET, Single-pool (Kt/V) was: [(1.25 ± 0.09) during first use and (1.19 ± 0.11) during twelfth uses]. For F80B, Single-pool (Kt/V) was: [(1.58 ± 0.21) during first use, and (1.50 ± 0.17) during fifteenth uses].[42 level II-3]

Similarly, Fleming et al. who conducted a cross sectional study involving 59 hospital haemodialysis patients in Australia using four types of hollow fibre dialysers (TAF 08,TAF 12, CA-90, and C-DAK 4000) reprocessed using Renalin reported that in vivo clearances of urea, creatinine and phosphate were not altered by reuse. However, there was a small but significant decrease in the ultrafiltration characteristics of used dialysers from a mean of 3.3 ml/h/mmHg on first use to 3.1 ml/h/mm Hg on the sixth use (t =2.41, P < 0.05).[43 level II-3]

In contrast, a prospective study conducted by Sherman et al. involving 34 dialysis units and 436 haemodialysis patients to assess dialysis delivery found that the mean delivered Kt/V for high reuse treatments was significantly lower than that for low reuse treatments (1.05 versus 1.10, P = 0.002). In their study, dialysers were reprocessed using formaldehyde in 23 centres (325 patients), Renalin in five centres (48 patients) and glutaraldehyde in six centres (63 patients). All patients underwent formal urea kinetic modelling monthly, usually for three sequential months. Dialysers were reprocessed and reused in the usual manner for each unit. For each patient, Kt/V urea for the treatment using the dialyser with the most reuses (mean, 13.8) was compared with the treatment using the dialyser with the fewest reuses (mean, 3.8). The prescribed Kt/V for the high and low reuse treatments was identical (1.21 in both groups). The decreased in delivered dialysis with formaldehyde reuse was highly statistically significant (1.02 versus 1.08; P = 0.002), but not significant for Renalin and gluteraldehyde reuse. The authors concluded that dialyser reprocessing significantly impairs dialysis delivery, an effect that may be related to the methods and procedures in individual dialysis centres.[44 level II-3]

b. Clearances of Large Molecular Weight Solutes

Cheung et al. reported the effect of bleach used in conjunction with formaldehyde, Renalin, or gluteraldehyde for reprocessing dialysers on β_2M clearance. For F80B dialysers, the rate of increased in β_2M clearance with reuse differed significantly (P < 0.001) among the three germicides. Bleach in conjunction with formaldehyde had the greatest effect on F80B dialysers. The β_2M clearance by F80B dialysers increased markedly through 20 reuses. The mean ± SEM rate of increased was greater during the initial seven reuses (3.32 ± 0.44 mL/min per reuse; P<0.001) than during the seventh through twentieth reuses (1.40 ± 0.26 mL/min per reuse; P < 0.001). The effectiveness of bleach in increasing β_2M clearance of F80B dialysers was lower when it was used in conjunction with Renalin (1.88 ± 0.26 mL/min per reuse) instead of formaldehyde. The β_2M clearance of F80B dialysers reprocessed using gluteraldehyde with bleach increased only by 0.84 ± 0.25 mL/min per reuse; P < 0.001 before June 15 1997, and by 0.55 ± 0.18 mL/min per reuse; P = 0.004 after June 15 1997. When bleach was used in conjunction with either formaldehyde or gluteraldehyde to reprocess CT190 dialysers, modest increased in β_2M clearance were observed (0.29 ± 0.11 mL/min per reuse; P = 0.011). The rate of increased in β_2M clearance did not differ significantly between the two aldehydes. When low-flux dialysers were reprocessed using any procedure that included bleach, there was a small but statistically significant increased in β_2M clearance during reuse (0.25 ± 0.07 mL/min per reuse; P < 0.001). Rate of increased in β_2M clearance did not differ significantly among formaldehyde, gluteraldehyde, and Renalin (all in conjunction with bleach), P = 0.075.[39 level II-1]

Leypoldt et al. in a crossover study involving six patients reported clearance of β_2M and dialysate total protein concentrations were low and not significantly different from zero for low flux dialysers during all uses. Clearances of β_2M were high for both types of high-flux dialysers (CT190G and F80A) on first use but decreased with reuse. The decreased in β_2M clearance at use number 15 was proportionately greater for CT190G dialyser (68%) than F80A dialyser (29%). Dialysate total protein concentrations were substantially larger for high-flux than low-flux dialysers during first use, but these concentrations decreased with increasing reuse, paralleling changes in β_2M clearance. The authors concluded that the observation showed that the maintenance of small solute clearances during reuse of high-flux dialysers does not ensure the maintenance of large solute clearance. Dialyser TCV of reprocessed highflux dialysers cannot be used to predict clearances of large solutes.[40 level II-3]

Kerr et al. reported the effect of prolonged use (up to 20 uses) of high-flux polysulfone dialysers reprocessed using peroxyacetic acid with or without bleach on β_2M clearance and retinol-binding protein (RBP). They found that there was small statistically significant decreased in percent reduction when use number 10 or number 20 was compared with use number one or two:[(71.8 ± 1.1%) during first use, (66.8 ± 1.5%) during tenth uses, and (66.8 ± 2.2%) during twentieth uses, P < 0.05], but not on comparing use number one with use number two. This decreased in percent reduction of β_2M by twentieth uses only amounted to a 7% reduction in β_2M removal. For RBP there was a significant decreased in the percent reduction when use number 20 was compared with use number one:[(18.6 ± 2.1%) during first use and (11.2 ± 2.4%) during twentieth uses, P < 0.05].[41 level II-3]

Quseph et al. reported that removal of β_2M decreased with reuse for both high-flux dialysers (AM-UP-75WET dialyser which contain 1.5 m^2 of regenerated cellulose membrane and F80B dialyser which contain 1.8 m^2 of polysulfone membrane) despite blood compartment volumes remains at 80% of their initial value. The change in β_2M removal was most marked for F80B dialyser. The predialysis to postdialysis reduction in β_2M concentration decreased significantly as the number of uses increased (P = 0.042).The reduction in β_2M concentration decreased from 30 ± 12% during the first use to 12 ± 10% during the tenth use (P < 0.05). Although the predialysis to postdialysis reduction in β_2M concentration also decreased with reuse of AM-UP-75WET dialyser (18.2 ± 9%, 19 ± 6%, and 12 ± 11% during the first, fourth, and twelfth uses respectively), the change was not significant, P = 0.276. The β_2M removal decreased to less than 90% of the initial value even though the blood compartment volume remained greater than 80% of its initial value 71% of the time with AM-UP-75WET dialyser and 65% of the time with F80B dialyser.[42 level II-3]

Matos et al. studied the effect of reuse on the permeability of low-flux membranes to solutes of different molecular weights especially regarding middle molecule. They studied two different types of low-flux membranes at reuses 0, 6, and 12 in five patients undergoing haemodialysis with the following combinations of membrane and sterilant; cellulose diacetate membrane and formaldehyde, polysulphone membrane and formaldehyde, cellulose diacetate membrane and peracetic acid, and polysulphone membrane and peracetic acid. The permeability of the membranes was assessed through the Hydraulic ultrafiltration coefficient (K_{UF}), Sieving coefficient for β_2M, and vitamin B12 and albumin concentrations in ultrafiltrate.

They found that after twelve reuses, TCV tended to be reduced in both cellulose diacetate and polysulphone dialysers irrespective of the sterilant used, but significance was only found for cellulose diacetate (P < 0.05 versus reuse 0). Cellulose diacetate dialysers reprocessed with either formaldehyde or peracetic acid showed reduction in K_{UF} (31%, P < 0.05 and 23%, P < 0.05%), respectively. A significant elevation in K_{UF} was found in polysulfone membranes reprocessed with peracetic acid (41%, P < 0.05), but no alteration in K_{UF} were found in polysulfone membranes reprocessed with formaldehyde. Cellulose diacetate membranes were intrinsically more permeable to β_2M than polysulfone membranes (sieving coefficient: 6.85 ± 2.53 versus 0.04 ± 0.02 x 10^{-2}, P < 0.001), which was not modified by any of the sterilants. Vitamin B_{12} levels in ultrafiltrate decreased to undetectable level in four of five samples collected after twelfth reuses in polysulfone membranes reprocessed with peracetic acid (90 ± 71 to 3 ± 8 pg/mL, P< 0.05), versus reuse 0. Albumin leakage occurred in two of five samples after the twelfth reuses, but only in polysulfone membranes reprocessed with peracetic acid. The authors concluded that our findings suggest that reuse of low-flux polysulfone dialysers reprocessed with peracetic acid is associated with structural damage of the membrane and reduced permeability to middle molecules.[45 level II-3]

6.1.3. CLINICAL EFFECTIVENESS

Four articles related to the clinical effectiveness of single use dialyser versus reuse dialyser were included in this review: one SR and three cohort studies. There was no RCT retrieved. The articles were published between 1994 and 2012.

Risk of bias

The SR by Galvao et al. on mortality risk is considered to have low risk of bias. The cohort studies included have unclear risk of bias whereby the two studies by Feldman et al. did not mentioned about blinding in the measurement of the outcome, while the study by Held et al. was unclear about blinding, control of confounding factors and follow-up of subjects.

a. Mortality

Galvao et al. conducted s systematic review on the effectiveness of dialyser reuse compared to single use in patients with ESRD. They searched MEDLINE, EMBASE, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Latin American and Carribean Centre on Health Sciences Information (LILACS), Scientific Electronic Library Online (SciELO), United States Renal Data System 2011 Annual Data Report (USRDS ADR), universities theses, and the annals of congress of major nephrology societies were searched. Grey literature was also searched. References of relevant articles were screened. Last literature search was conducted in January 2012.Four pairs of researches independently selected trials for inclusion. Data from each included trial were extracted by one of the three researchers and the other two confirmed the extraction. The quality of the included studies was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[46 level II-1]

A total of 1,190 studies were retrieved, and 14 were included in the review. The studies included in the review were: Held 1987, Held 1994, Feldman 1996, Collins 1998, Feldman 1999, Ebben 2000, Port 2001, Collins 2004, Lowrie 2004, Fan 2005, Chuang 2008, Lacson 2011, Bond 2011, and USRDS 2011. The number of patients included in the review was 956,807. Only one study (Chuang, 2008) had a sample size of less than 1,000. The largest sample size was from the USRDS 2011, where 245,538 patients were treated in 2009; 110,299 on reuse dialysers and 135,239 on single use dialysers. Nine of the studies were retrospective cohort, four prospective cohort and one crossover design. Thirteen of the studies were conducted in U.S.A. while one study was conducted in Taiwan. The disinfectants used on dialyser reprocessing were hypochlorite, formaldehyde, glutaraldehyde, and peracetic acid. Four of the studies used conventional dialyser membrane, five studies used conventional and synthetic dialyser membrane, three studies used synthetic membrane and two studies did not report on the type of membrane used. The average number of reuses ranged from 2.54 to 15. Eight studies involved hospital and free standing dialysis facilities, five studies involved freestanding dialysis facilities, while one study involved hospital dialysis facility. The evidence was classified as very low using the GRADE approach.[46 level II-1]

The majority of the studies revealed no statistically significant differences in mortality between dialyser single use and dialyser reuse. The most comprehensive provider level comparison, the USDRS ADR 2011 (245,538 patients treated in 2009, adjusted for the same confounding), found similar results in Standardised Mortality Ratio (SMR) of patients treated by providers that employ only single use (Fresenius and DCI) and patients treated on DaVita, considered as reuse (≥ 75% patients treated with reuse of dialysers). However, patients treated on DaVita had a statistically significant slight reduction in SMR: SMR = 0.97; 95% CI: 0.96 to 0.99. Even in studies where statistically significant difference was identified, it was not observed in all groups and varied by the type of disinfectant, the length of follow-up and the health care facility type as shown in Table 3 and Table 4. In the study by Chuang et al., the single use dialysers significantly increased the risk of death compared to reuse, but different inclusion criteria were applied for patients in the reuse and single use groups resulting in statistically significant healthier patients profile in the reuse group. [46 level II-1]

Table 3. Mortality risks of single use dialysers compared to reuse dialysers

	Subgroups of analysis					
Study	**Disinfectant type**	**Facility type**	**Other subgroups**	**Relative Risk**	**95% CI**	**P value**
Lowrie, 2004	Formaldehyde, peracetic acid, glutaraldehyde, acetic acid, heat based, hypochlorite		Day 0	HR 0.95	0.90-1.01	n.r
			After 30 days	HR 0.95	0.88-1.01	0.089
			After 60 days	**HR 0.92**	**0.86- 0.98**	**0.011**
			After 90 days	**HR 0.92**	**0.84- 0.99**	**0.004**
			After 120 days	**HR 0.92**	**0.84- 0.97**	**0.005**
Chuang, 2008	4% peracetic acid mixture (peracetic acid, hydrogen peroxide, acetic acid)	Hospital		**OR 2.94**	**1.56-5.55**	**0.0009**
Lacson, 2011	Peracetic acid mixture	Freestanding		**R 0.74**	**0.56-0.89**	**0.01**

Note: n.r. = not reported

Table 4. Mortality risks of reuse dialysers compared to single use dialysers

	Subgroups of analysis					
Study	**Disinfectant type**	**Facility type**	**Other subgroups**	**Relative Risk**	**95% CI**	**P value**
Held, 1987			Multiple uses started at or prior to 1980	0.88	n.r.	<0.03
			Multiple uses started after 1980	1.01	n.r.	<0.88
Held, 1994	Formaldehyde			1.06	0.99-1.14	0.088
	Glutaraldehyde			**1.17**	**1.04-1.31**	**0.010**
	Peracetic acid			**1.13**	**1.06-1.21**	**<0.001**
Feldman, 1996	Formaldehyde	Hospital		1.06	0.98-1.15	0.12
		Freestanding		1.03	0.96-1.10	0.45
	Glutaraldehyde	Hospital		1.09	0.71-1.67	0.70
		Freestanding		1.13	0.95-1.35	0.18
	Peracetic acid	Hospital		0.95	0.85-1.06	0.40
		Freestanding		**1.10**	**1.02-1.18**	**0.02**
Collins, 1998	Formaldehyde	Hospital		1.15	0.86-1.55	n.r.
		Freestanding		0.82	0.72-0.93	n.r.
	Glutaraldehyde	Hospital		1.09	0.74-1.59	n.r.
		Freestanding		1.03	0.80-1.33	n.r.
	Peracetic acid	Hospital		0.94	0.67-1.32	n.r.
		Freestanding		**0.83**	**0.72-0.96**	**n.r.**
Feldman, 1999	**Formaldehyde, Glutaraldehyde, and Peracetic acid**			**1.25**	**1.03-1.52**	**0.023**
Ebben, 2000	Formaldehyde, Glutaraldehyde, and Peracetic acid			n.r.	n.s.	n.r.
Port, 2001	Formaldehyde, Glutaraldehyde, Peracetic acid and hypochlorite			0.96	0.86-1.08	0.51
Collin, 2004	Formaldehyde			1.01	0.92-1.11	n.r.
	Glutaraldehyde, Peracetic acid, and hypochlorite			n.r.	n.s.	n.r.
Fan, 2005			All patients	HR 0.98	0.94-1.02	0.266
Bond, 2005		Freestanding		HR 1.04	0.97-1.12	n.s.
USRDS, 2011			Fresenius	SMR 1.01	0.99-1.02	
			DaVita	**SMR 0.97**	**0.96-0.99**	
			DCI	SMR 0.91	0.91-1.01	

Note: n.r. = not reported, n.s. = not reported but informed to be not significant

b. Hospitalisation

The risk for hospitalisations between single use dialyser and reuse dialyser was assessed in three studies.[47-49] Feldman et al. conducted a cohort study of hospitalisation rates among 27,264 ESRD patients beginning heamodialysis in the U.S.A. in 1986 and 1987 to determine if reuse of haemodialysers is associated with higher rates of hospitalisation. Of the 27,264 patients studied, 18,679 were treated in freestanding dialysis facilities and 8,585 patients were treated in hospital-based facilities. They found that among patients in freestanding facilities, reuse dialysis was associated with higher hospitalisation rates from any cause than single use dialysis: RR = 1.08; 95% CI: 1.02 to 1.14, P = 0.01. This higher rate of hospitalisation was observed with dialyser reuse using peracetic acid/acetic acid: RR = 1.11; 95% CI: 1.04 to 1.18, P < 0.01, and formaldehyde: RR = 1.07; 95% CI: 1.00 to 1.14, P = 0.04, but not gluteraldehyde: RR = 1.00; 95% CI: 0.89 to 1.13, P = 0.97. Adjusted mean hospitalisation rates for patients exposed to reuse dialysis and for patients expose to single use dialysis in freestanding dialysis facilities were 2.25/ year and 2.19/year, respectively. There was no difference among hospitalisation rates in hospital based facilities reprocessing dialysers with any sterilant and those not reprocessing.[47 level II-2]

Analyses of hospitalisation for causes other than morbidity associated with dialysis vascular access yielded results similar to those of the analysis of hospitalisation for any cause. Among patients in freestanding facilities, reuse dialysis was associated with higher hospitalisation rates than single use dialysis: RR= 1.06; 95% CI: 1.00 to 1.13, P = 0.04. Hospitalisation in freestanding facilities reusing dialysers with formaldehyde was not different from hospitalisation in facilities not reusing. However, reuse with peracetic acid / acetic acids was associated with higher rates of hospitalisation than formaldehyde: RR = 1.08; 95% CI: 1.03 to 1.15, P< 0.01. Analysis of hospitalisation for blood-borne infection failed to detect any significant relationships between dialyser reuse or specific sterilants and the rate of hospitalisation in either free-standing or hospital-based facilities.[47 level II-2]

Feldman et al. conducted another cohort study to determine whether the associations between reuse of haemodialysers and higher rates of death and hospitalisations persist after adjustment for comorbidity. The study involved 1,491 U.S.A. chronic HD patients beginning treatment in 1986 and 1987. The impact of dialyser reuse was compared across three survival models: an unadjusted model, a "base" model adjusted for demographics and renal diagnosis, and an "augmented" model additionally adjusted for comorbidities. They found that the relationships between dialyser reuse and hospitalisation were similar with and without adjustment for age, gender, diagnosis, or baseline comorbidities. The relative rate of hospitalisation for reuse overall was between 35% and 40% greater than for single use: unadjusted model: RR = 1.40; 95% CI: 1.17 to 1.67, P < 0.001, base model: RR = 1.35; 95% CI: 1.17 to 1.56, P < 0.001, and augmented model: RR= 1.37; 95% CI: 1.17 to 1.58, P < 0.001.[48 level II-2]

Compared with single use, the rates of hospitalisation with either the combination of peracetic and acetic acid or formaldehyde were stable across the three models. There was a 37% to 42% higher rate of hospitalisation with the combination of peracetic and acetic acid compared with single use: unadjusted model: RR = 1.42; 95% CI: 1.17 to 1.74, P < 0.001, base model: RR= 1.37; 95% CI: 1.13 to 1.66, P = 0.001, and augmented model: RR= 1.40; 95% CI: 1.17 to 1.66, P < 0.001. There was between 21% to 25% higher rate with formaldehyde compared with single use: unadjusted model: RR = 1.25; 95% CI: 1.06 to 1.47, P = 0.009, base model: RR =1.21; 95% CI: 1.05 to 1.41, P = 0.009, and augmented model: RR = 1.25; 95% CI: 1.09 to 1.43, P = 0.002.[48 level II-2]

Similarly, Held et al. reported that patients treated in "low-flux" freestanding dialysis units that disinfected dialysers with peracetic acid mixture and glutaraldehyde had higher risk of hospitalisation compared with patients treated in non reuse units, while patients treated with formaldehyde experienced rates of hospitalisation that were similar to non reuse units. The adjusted relative risk was 1.11, P < 0.01 for peracetic acid mixture, 1.12, P < 0.03 for glutaraldehyde, and 1.04, P = 0.29 for formaldehyde.[49 level II-2]

6.1.4. ECONOMIC EVALUATION

There were limited retrievable studies related to the cost-effectiveness of single use dialysers versus reuse dialysers. In this review, we included one cost-utility analysis, one cost-minimisation analysis and two cost-analysis studies. Two of the studies were conducted in Canada, while the rest were conducted in Taiwan and Saudi Arabia.

An economic evaluation (cost-utility analysis) was performed in Canada in 2002 to evaluate the cost-effectiveness of reusing haemodialysers for patients with kidney failure on dialysis employing either a heated citric acid or formaldehyde sterilisation method, in comparison to the standard practise of single use dialysis. A meta-analysis of all relevant studies was performed to determine whether haemodialyser reuse was associated with an increased relative risk of mortality and hospitalisation. A decision tree was constructed to model the effect of three different dialysis strategies (single use dialysis, heated citric acid, and formaldehyde dialyser reuse) on the costs and quality-adjusted life expectancy of "typical" haemodialysis patients. The cost of the ESRD care, survival data, and patients utilities were estimated from published sources. There was evidence of a higher risk of hospitalisation for haemodialyser reuse compared with single use dialysis. Depending on the assumptions used, the cost saving that could be expected by switching from single use dialysis to heated citric acid reuse were small ranging from CAN $ 0 to Can $ 739 per patient per year. A 320-patient haemodialysis unit using lower cost heated citric acid reuse and RR of mortality and hospitalisation assumed to be one, with an average reuse number of 13, could save CAN $ 739 per patient per year. This does not take into account the extra costs that a program considering reuse would face if the reuse facility were located in a different site than the dialysis facility. In addition, this saving may be more than offset by the extra expenditure resulting from an increased risk of hospitalisation due to haemodialyser reuse.[50]

In contrast, a cost minimisation analysis which considered the outcomes of the alternative programs of interest to be identical, conducted in Canada in 1993, suggested potential cost saving of CAN $ 3,629 per patient per year with five reuses using formaldehyde.[51] Similarly, a cost analysis conducted in Taiwan comparing the direct cost of single use dialyser and reuse dialyser (including cost of reprocessing), reported that annual cost of hollow fibre for reuse was reduced by NT$ 17,565.6 (US $ 540.48) per patient per year.[52] In another cost analysis conducted in Saudi Arabia, comparing the direct cost of high-flux single use dialyser and reuse dialyser (excluding reuse machine, computer system and personnel), reported a total cost savings of 53%.[53]

6.1.5. ORGANIZATIONAL

a. Training

The reprocessing process entails multiple steps, from receiving a used dialyser to sending it back out to be reused by a patient, each with the potential for human error and process breakdown. Hence, personnel shall possess adequate education, training, or experience to understand and perform procedures outlined by the individual dialysis facility relevant to the facility's multiple use program.[7,8,9,20] The Guideline on HD Quality and Standards by the Medical Development Division, Ministry of Health in 2012, states that the person in charge of a haemodialysis centre shall be a nephrologist or a physician or registered medical practitioner who have completed not less than 200 hours of recognised training in haemodialysis treatment, while the registered nurse or medical assistant shall have at least six months training and experience in haemodialysis. Infection control training and education is recommended for both staff members and patients (or their family and care givers).[9]

b. Separation practices for HBsAg-positive patients

In the U.S.A. among centres with ≥ one HBsAg positive patients, the incidence of HBV infection among patients was significantly lower in centres where HBsAg positive patients received dialysis in a separate room and a dedicated machine than in centres using no separation practices or only a separate machine in 1976,1980,1983,1989, 1992, and1993 but not in 1990, 1991, 1994 to 1997.[27-30]

c. Dialysis room and dialyser reprocessing strategies for anti-HCV-positive patients

A survey was conducted among hospital directors of 71 HD units in Portugal in August 1994 to evaluate the impact of dialysis room and reuse policies on the incidence of HCV infection. Information for the years 1991, 1992 and 1993 was requested with respect to HCV infection. Overall, data from 5,774 patient-years were available for analyses. They found that the incidence of HCV infection was lowest among units that used dedicated machines: OR = 0.22; 95% CI: 0.11 to 0.43, P <0.001, or separate rooms for anti-HCV-positive patients: OR = 0.46; 95% CI: 0.29 to 0.73, P = 0.001. Among units that reprocess dialysers, the incidence of HCV infection was lowest in:(i) units that used separate rooms for reprocessing dialysers from anti-HCV-positive patients: OR = 0.06; 95% CI: 0.01 to 0.22, P< 0.001, and (ii) ban on reuse of dialysers from anti-HCV-positive patients: OR = 0.27; 95% CI: 0.13 to 0.59, P < 0.001.[33]

6.1.6. LEGAL IMPLICATION

The requirement for reuse of dialyser in private healthcare facilities in Malaysia is included in the Malaysian Private Healthcare Facilities and Services Act 1998, Part XXII: Special requirements for haemodialysis facilities and services. It states that patients with positive HBsAg, positive HCV antibody or positive HIV antibody shall be dialysed in isolation rooms that are separate from other patients. Dialysers from patients with positive HBsAg, positive HCV antibody or positive HIV antibody may not be reused and if the dialysers are reused or intend to be reused, the licensee or person in charge of a private HD centre or a private hospital providing hospital HD centre shall ensure that such dialysers (a) are reprocessed using a machine separate from those used for reprocessing dialysers; and (b) be stored separate from the dialysers, of non-infected patients.[8]

The presence of any program with a potential risk of lapses or breakdown specifically one that involves potentially harmful or corrosive substances or equipment, poses a litigation risk. However, we did not retrieve any article on litigation associated with dialyser reprocessing. There was an article by Hallquist SG. on legal consequences of disposable dialyser reuse. The article discusses the potential legal liability for adverse effects resulting from reuse of disposable dialysis equipment.[54]

6.1.7. ENVIRONMENTAL

The dialysis procedure creates a considerable amount of waste.[55] Therefore, waste management needs to be at the heart of any modern dialysis provider system. Reuse of dialysers raises a number of important environmental concerns. Spillage of heated contaminated water uses for dialyser rinsing into the sewer system, increased chemicals and disinfectants waste, increased plastic waste from packaging materials used for reuse chemicals, and additional waste generated from disposable items such as masks, gloves, test strips, plastic aprons, and labels, are all potential pollutant associated with reuse. The authors predicted that approximately 6.4 million gallons of peracetic acid and 1 million gallons of aldehydes are released into the environment every year because of reuse in the U.S.A. based on estimates of dialyser reuse in 2005. Single use of dialysers also poses a challenge to the dialysis community of formulating plans for effective solid waste management with the minimal adverse impact to the environment.[11]

6.2. PART B (LOCAL ECONOMIC EVALUATION)

Single use was found to be more expensive but more effective than reuse (Figure 2). However, the ICER was found to be above the threshold of cost-effectiveness (Table 2).Close inspection on scatter plot would shows that single use is either in quadrant 1 (trade-off) and quadrant 4 (dominated) of cost- effectiveness plane (Figure 3).

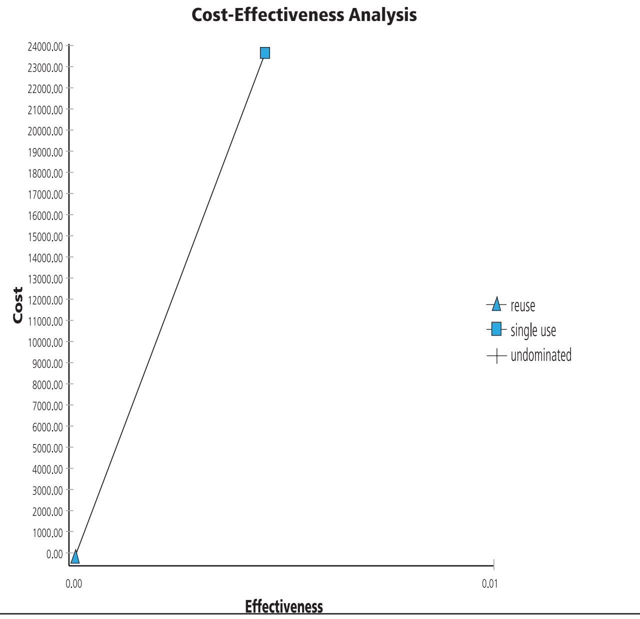


Figure 2: Deterministic cost- effectiveness plane of single use versus reuse

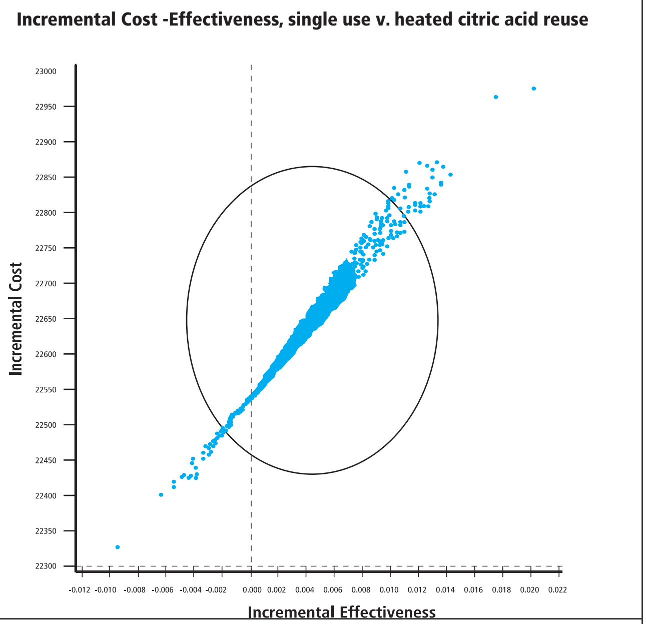


Figure 3: Probabilistic cost- effectiveness plane of single use versus reuse

Table 2: Results of deterministic cost effectiveness analysis

STRATEGY	AVERAGE COST-EFFECTIVENESS RATIO (MYR)	AVERAGE COST (MYR)	AVERAGE EFFECTIVENESS (QALY)	INCREMENTAL COST (MYR)	INCREMENTAL EFFECTIVENESS (QALY)	ICER (COST/QALY)
Peracetic acid reuse	27094.88	51443.24	1.899	0	0	0
Single use	38928.08	74087.02	1.903	22643.78	0.005	4983655

Based on the available evidence, there is a 100% probability that using reuse dialyser is more cost-effective (Figure 4). Inspection of single variable effect on the conclusion found that the results' direction would change with more expensive reuse dialyser, or cheaper single use dialyser.
The direction of results are sensitive to the probability, cost and utility of transplant (Figure 5).

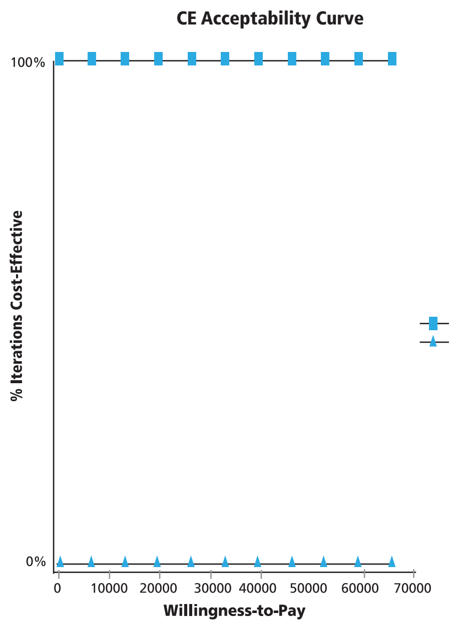


Figure 4: Cost- effectiveness acceptability curve of single use

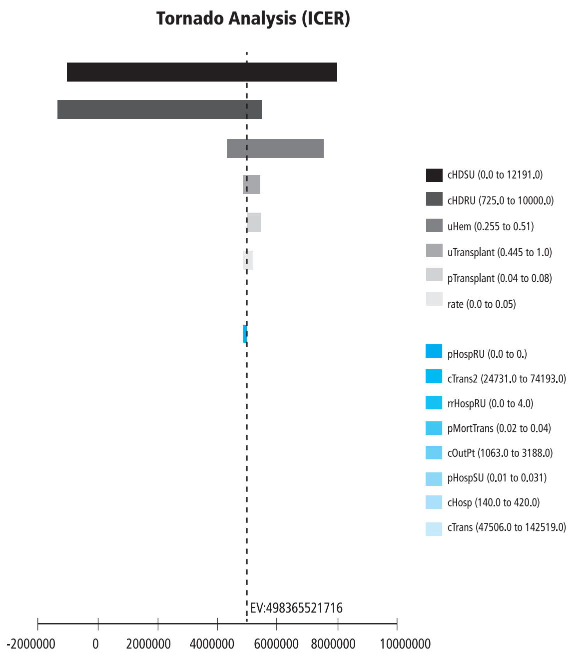


Figure 5: Tornado diagram for variables impact on ICER

Threshold analysis (Figure 6) shows the cost of single use haemodialyser on the x-axis and the incremental cost on the y-axis. The breakeven point where both single use dialyser and reuse dialyser expected value are equal is MYR 1,418. Below this cost, the single use dialyser strategy would be favoured. As this threshold value is more than five times smaller than the baseline, the analysis is robust with respect to the assumed cost.

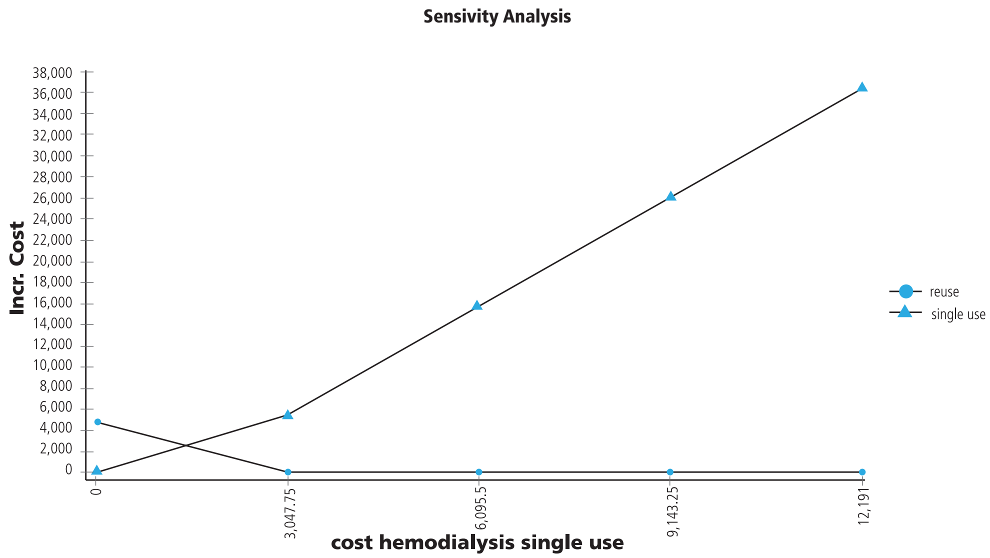


Figure 6: One-way sensitivity analysis on cost of single use dialyser.

7 DISCUSSION

There was no HTA report on single use dialyser versus reuse dialyser or vice versa. There was a Cochrane protocol on dialyser reuse for people with end-stage kidney disease requiring haemodialysis in The Cochrane Library 2012, Issue 10.[56] Data from CDC have linked dialyser reuse to pyrogenic infections and outbreaks of bacterial infection in the 1980s and 1990s due to breakdown in the reprocessing technique.[24] Patients who reused dialysers were found to have 28% higher risk of septicaemia than patients who did not reuse dialysers and had a ninefold greater risk of death from septicaemia.[26] In Malaysia, in 2010, 90% of patients undergoing haemodialysis were using reuse dialysers. Death from infection has increased over the last four years and has became the second most common cause of death in 2010, accounting for 24% of all death.[4] However, the link between reuse dialysers and septicaemia could not be ascertained.

Although viruses such as HBV, HCV and HIV pose potential infection risk to employees and patients in haemodialysis centres, Tokars et al. reported that reuse of diaysers was not associated with increased risk of HBV or HCV infection in either patients or staffs.[27-31] However, outbreaks of HBV infection were reported in the U.S.A. as a result from: (i) failure to identify and isolate HBV-infected patients during haemodialysis, (ii) sharing of staff, equipment, and supplies among patients, and (iii) failure to vaccinate susceptible patients against hepatitis B as advocated by guidelines.[32] The CDC in their Recommendations for Preventing Transmission of Infections among Chronic Haemodialysis Patients in 2001, states that dialysers should not be reused on HBsAg-positive patients because HBV is efficiently transmitted through occupational exposure to blood. Hence, reprocessing dialysers from HBsAg-positive patients might place HBV-susceptible staff members at increased risk for infection. This is in line with the findings that in some studies the incidence of HBV infection among patients was found to be significantly lower in centres where HBsAg positive patients received dialysis in a separate room and a dedicated machine than in centres using no separation practices or only a separate machine.[27-30] In Portugal, among units that reprocess dialysers, the incidence of HCV infection was lowest in units that used separate rooms for reprocessing dialysers from anti-HCV-positive patients, or ban on reuse of dialysers from anti-HCV-positive patients.[33]

The argument that dialysers should be reused in order to improve blood-membrane biocompatibility is less compelling now than in the past since synthetic membranes with improved blood membrane biocompatibility are now widely available. In the U.S.A., the new dialyser syndrome (first-use syndrome) reported a decline from 43% in 1984 to 28% in 1994. It was reported most frequently by centres using regenerated cellulose and cuprophan membranes.[27-28] Moreover, anaphylactoid reactions have been attributed to reuse of dialysers.[35] Intradilaystic symptoms were found to be similar in patients on single use dialysers compared to reuse dialysers in two studies but was found to be significantly less frequent during the period in which dialysers were reuse in one study.[35-38]

It is often assumed that dialyser performance is not altered when dialyser reprocessing is performed according to the AAMI standards and recommended practices. The quantitative criterion recommended by AAMI is that TCV or fibre bundle volume should not fall below 80% of its original value, assuring that urea clearance of the dialyser stands within 90% to 100% of the original level.[57] However, this is may not be true. Dialyser reprocessing and reuse can affect HD delivery. Several studies have shown that there were no statistically significant differences in small molecular weight solute clearances (urea, creatinine, phosphate) with the number of reuse for both high-flux and low-flux dialysers.[40-43] The HEMO study confirmed minimal decreases (approximately 1% to 2%) urea clearances per 10 reuses with a variety of dialysers and reuse techniques.[39] However, the study by Sherman et al. did not support the conclusion that 80% fibre bundle volume ensures acceptable urea clearances. They showed that the mean Kt/V delivered for high reuse treatments was significantly lower than that for low reuse treatments (1.05 versus 1.10, P =0.002).[44] According to the 18th Report of The Malaysian Dialysis and Transplant Registry 2010, haemodialysis patients with Kt/V ≥ 1.6 had the lowest adjusted hazard ratio for mortality (HR =0.91; 95% CI: 0.85 to 0.97).[4] To ensure adequate dialysis delivery, the Haemodialysis Quality and Standards, Medical Development Division, Ministry of Health, 2012, recommended that ≥ 95% of patients have prescribed Kt/V >1.3 and ≥ 90% of patients have delivered Kt/V > 1.2.[9]

Clearances of larger solutes were also affected. The change in clearance varies depending on dialyser types and reuse reagents. β_2M clearance was low and not altered appreciably by reuse of low-flux dialysers.[39-40] Clearance of β_2M was high for high-flux dialysers. However, reuse of high-flux dialysers can have substantial impact on β_2M and RBP clearances whereby β_2M and RBP clearances decreased with reuse.[39-42] When bleach was included in germicide-based reprocessing cycles, β_2M clearances tend to increase.[39] The findings showed that maintenance of small solute clearance during reuse of high-flux dialysers does not ensure the maintenance of large solute clearance even though the dialyser TCV remained greater than 80%.[40,42]

Mortality and morbidity in relation to reuse versus single use have been investigated. However, there were no longitudinal studies of clinical outcomes that have randomly assigned patients to single use or reuse of dialysers. Hence, inferences have been derived from observational studies. The SR by Galvao et al. involving 14 observational studies reported no significant differences for the superiority or inferiority of dialyser reuse versus single use when assessing the mortality of patients with ESRD.[46] However, among patients in freestanding facilities, reuse of dialysers was associated with higher hospitalisation rates from any cause than patients on single use dialysers. The higher rate of hospitalisation was observed with dialyser reuse using peracetic acid /acetic acid or formaldehyde.[47-48]

One of the main reasons for reusing dialysers is due to economic. Indeed, the cost of a single dialyser multiplied by the number of haemodialysis treatments per year is a large expense for the dialysis provider compared to the cost of only one dialyser per patient per month, even with the added cost of reprocessing. However, the economic evaluation of whether or not to reprocess dialysers is similar to all comparative cost analyses: evaluating the cost difference between single use and reuse strategies. "Cost" refers to the total cost and includes the direct costs of products, the direct cost of production, indirect cost and opportunity costs associated with each strategy.[15]

A cost-utility analysis performed in Canada in 2002 reported the cost saving that could be expected by switching from single use dialysis to heated citric acid reuse were small ranging from CAN $ 0 to CAN $ 739 per patient per year. Since the study was conducted 13 years ago and using heated citric acid which is cheaper compared to Renalin (currently, most commonly use germicide), the cost saving may no longer be as great since single use dialysers have become significantly less expensive. These discrepancies highlight the need to re-examine the extent of economic benefit with reuse of dialysers in the context of increased availability of cheaper single use high-flux dialysers and the rising cost of personnel, space, equipments and consumables.[50]

The local economic evaluation study evaluated cost-effectiveness of single use dialyser compared to reuse dialyser in public hospital setting in Malaysia. Single use dialyser was found to be less cost-effective than reuse dialyser. Further analysis from the breakeven point shows that single use dialyser can be cost-effective if its cost per run is less than MYR 9.09 (MYR 1,418 / (3 times per week * 52 weeks per year). This would means that the maximun unit cost (that would make it cost-effective) for single use dialyser is MYR 1.99, after excluding the cost of biohazardous waste diaposal and diasafe filter. This results might be a reflection of the minimal benefit of mortality and hospitalisation between single use and reuse that might not be able to offset the higher cost of single use dialyzer.[1] However, it should be noted that the model has ignore possible effect of infectious disease contamination and associated building cost to accommodate high risk infected dialyser. The building costs were not incorporated in the cost data source[2], but could possibly increase the cost of reuse dialyser due to mandatory storage facility requirement for its use. This complex model and costing could be explored in future modelling work. The model is also limited by lack of variance reported for costs and local utility estimate [2-4,7]- hence, preventing the study to explore joint effect of outpatient, hospitalisation, renal transplant and dialyser cost and utility to the results. This is important considering that the cost to treat kidney transplant patient particularly after the first year and utility for haemodialysis could change the direction of the results.

Health hazards associated with the use of germicides are important considerations in dialyser reuse. However, there was no retrievable evidence on the cumulative and long-term effects of chronic, low-dose exposure to reuse reagents (formaldehyde, hydrogen proxide, sodium hypochlorite, glutaraldehyde and peracetic acid).

The dialysis procedure creates a considerable amount of waste: both single use and reuse practices.[11,54] Hence, efforts should be made to compare the environmental impacts of single use and reuse practices in the future research. The reprocessing process entails multiple steps, each with the potential for human error and process breakdown. The reprocessing operations will become absolute once a facility switches to single use. Hence, making the dialysis operation less risky, more convenient, and alleviates medico-legal risks.[15]

Limitations

The systematic review of literature has several limitations. There were no RCT conducted to assess the mortality and morbidity related to single use dialyser and reuse dialyser practices. The observational studies mostly have unclear risk of biases. Most of the studies were conducted in the 1980s and 1990s. Hence, there may be differences in the types of dialysers, the germicides used and the reprocessing practice compared to the current practice. Generalizability and international comparisons of economic evaluations are very limited. Although there was no restriction in language during the search but only English full text articles were included in the report.

8 CONCLUSION

8.1. PART A (SYSTEMATIC REVIEW OF LITERATURE)

8.1.1. Safety of single use dialyser versus reuse dialyser

- There was fair level of evidence to suggest that:
    - Inadequate dialyser reuse practices were associated with outbreaks of bacterial infection and pyrogenic reactions.
    - Patients who reused dialysers were found to have 28% higher risk of septicaemia than patients who did not reuse dialysers and had a ninefold greater risk of death from septicaemia.
    - Reuse of dialyser was not associated with increased risk of HBV and HCV infection in either patients or staffs. However, (i) failure to identify and isolate HBV-infected patients during haemodialysis, (ii) sharing of staff, equipment, and supplies among patients, and (iii) failure to vaccinate susceptible patient were associated with outbreaks of HBV infection.
    - The incidence of new dialyser syndrome (first-use syndrome) has declined and was associated with regenerated cellulose and cuprophan membranes.
    - Reuse of hollow-fibre dialysers may be associated with anaphylactoid reactions.
- The evidence on intradialytic symptoms was inconclusive.
- The cumulative and long-term effects of chronic, low-dose exposure to reuse reagents (formaldehyde, hydrogen peroxide, sodium hypochlorite, glutaraldehyde and peracetic acid) cannot be determined.

8.1.2. Changes in membrane integrity

- There was fair to good level of evidence to suggest that small molecular weight solutes (urea, creatinine and phosphate) clearance were slightly greater for high- flux dialysers than low-flux dialysers. There was a trend for urea, creatinine and phosphate clearance to decrease with reuse for both high-flux and low-flux dialysers but these differences were not statistically significant.

- There was limited fair level of evidence to suggest that there was a small decline in dialysis dose (0.05 Kt/V units) when the mean frequency reuse was 3.8 to 13.8 times.

- There was fair to good level of evidence to suggest that clearance of large molecular weight solutes ($β_2$M, RBP) was affected by reuse practices. $β_2$M clearance was low and not altered appreciably by reuse of low-flux dialysers. Clearance of $β_2$M was high for high-flux dialysers. However, clearance of $β_2$M and RBP for high-flux dialysers decreased with reuse. When bleach was included in germicide-based reprocessing cycles, $β_2$M clearances tend to increase. Even though the dialysers TCV remained greater than 80%, reuse of high-flux dialysers does not ensure the maintenance of large solute clearance.

8.1.3. Clinical Effectiveness

- There was good level of evidence to suggest that there were no statistically significant differences in mortality between dialyser single use and dialyser reuse.

- There was fair level of evidence to suggest that reuse of dialysers was associated with higher hospitalisation rates from any cause. The higher rate of hospitalisation was observed with dialyser reuse using peracetic acid / acetic acid or formaldehyde.

8.1.4. Economic evaluation

- A cost-utility analysis performed in Canada in 2002 reported the cost saving that could be expected by switching from single use dialysis to heated citric acid reuse were small ranging from CAN $ 0 to CAN $ 739 per patient per year.

8.1.5. Organizational

- Reprocessing process entails multiple steps. Hence, personnel shall possess adequate education, training, or experience to understand and perform procedures outlined by the individual dialysis facilities.

- There was evidence to suggest that separation practices and ban on reuse of dialyser lower the incidence of HBV or HCV infection among patients.

8.1.6. Legal implication

- The requirement for reuse of dialyser in private healthcare facilities is included in the Malaysian Private Healthcare Facilities and Services Act 1998, Part XXII: Special requirements for haemodialysis facilities and services.

8.1.7. Environmental

- The dialysis procedure creates a considerable amount of waste (by single use or reuse practices). Hence, waste management needs to be part of dialysis provider system.

8.2. PART B (LOCAL ECONOMIC EVALUATION)

Reuse seemed to be more cost-effective than single use dialyser.

9 RECOMMENDATION

Single use dialyser should be used for those with infectious diseases such as Hepatitis B, Hepatitis C, Hepatitis B & C co-infection or HIV infection, subjected to the availability of resource. Further economic evalution using more complex model is advocated to determine the cost-effectiveness of using single use dialyser for all dialysed patients.

In line with the Ministry of Health guidance on Haemodialysis Quality and Standards and the Report of the Malaysian Dialysis & Transplant Registry where manual dialyser reprocessing system reported significantly higher risk for HCV seroconversion. Hence, automated reprocessing system for reuse of dialyser is advocated.

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Appendix 1

HIERARCHY OF EVIDENCE FOR EFFECTIVENESS STUDIES

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)

Appendix 2

PTK – FM – 02

HEALTH TECHNOLOGY ASSESSMENT (HTA) PROTOCOL SINGLE USE DIALYSER VERSUS REUSE DIALYSER

1. BACKGROUND INFORMATION

End stage renal disease (ESRD) or end stage kidney disease (ESKD) can be defined by the requirement for life-saving dialysis or kidney transplantation. According to the Bulletin of World Health Organization (WHO) 2007, worldwide the number receiving renal replacement therapy (RRT) which includes dialysis (haemodialysis and peritoneal dialysis) and kidney transplant is estimated at more than 1.4 million with incidence growing by approximately 8% annually. The increase is attributed to population ageing, type 2 diabetes mellitus and hypertension which are the key risk factors for chronic kidney disease. However, due to the expensive nature of RRT, treatment of ESRD is largely the domain of high income countries.

Renal replacement therapy in Malaysia has shown exponential growth since 1990. According to the 18th Report of The Malaysian Dialysis and Transplant Registry 2010, dialysis acceptance rates increased from 88 per million population in 2001 to 170 per million population in 2009. Dialysis prevalence rate more than doubled over the last 10 years, from 325 per million population in 2001 to more than 800 per million population in 2010. The number of dialysis patients in Malaysia has tripled in 10 years from 7,837 in 2001 to 21,245 in 2009. The number of haemodialysis centres for the whole of Malaysia increased from 208 in 2001 to 581 in 2010 giving a rate of 9 per million population in 2001 and 21 per million population in 2010. The Ministry of Health (MOH) provided dialysis to 30% of patients, non-governmental organizations (NGO) to 28% and the private sector to 40% of all dialysis patients. Fifty seven percent of patients on dialysis were funded by the government, 10% by NGO, 22% were self funded, 1% subsidised by employer and 10% others. The proportion of new ESRD patients with diabetes was 56% in 2010.

The annual death for haemodialysis patients was 11.2% and cardiovascular disease remained the main cause of death accounting for 34% of all death while infection has increased over the last four years and became the second most common cause of death in 2010, accounting for 24% of all deaths. Between 2001 and 2010, the annual prevalence of patients with Hepatitis B ranges from 4% to 6% in haemodialysis while the prevalence of Hepatitis C in haemodialysis patients continues to decline and was 7% in 2010.The cumulative risk of sero-conversion to HBsAg positive among sero-negative patients at entry into dialysis was 1.31% at seven years while for HCV was 3.16%. It was reported that centres which still use manual dialyzer reprocessing systems run significantly higher risk of seroconversion.

Haemodialysis is a method of removing waste products such as creatinine and urea, as well as free water from blood when the kidneys are in renal failure. The haemodialysis machine pumps the patient's blood and the dialysate through the dialyser. The dialyser is the piece of equipment that actually filters the blood. Almost all the dialysers in use today are of hollow-fibre variety.

Dialyser membranes come with different pore sizes. Those with smaller size are called "low-flux" and those with larger pore sizes are called "high-flux". Dialyser membranes used to be made primarily of cellulose which was not biocompatible and are no longer in use, whereas, cellulose acetate and modified cellulose dialysers are still in use. Another group of membranes is made of synthetic materials using polymers such as polyarylethersulfone, polyamide, polyvinylpyrrolidone, polycarbonate and polyacrylonitrile. These synthetic membranes activate complement to a lesser degree than unsubstituted cellulose membranes. Synthetic membranes can be made of either low-or-high flux configuration, but most are high-flux. Nanotechnology is being used in some of the most recent high-flux membranes to create a uniform pore size. The goal of high-flux membranes is to pass relatively large molecules such as beta-2-microglobulin but not to pass albumin.[5] High flux dialyser are usually used following recommendation by the nephrologists for certain types of patients such as those with bone problems or having aluminium toxicity.

Dialysers come in many different sizes. A larger dialyser with a larger membrane area will usually remove more solutes than a smaller dialyser especially at high blood flow rate. The dialyser may either be discarded after each treatment or be reused. Dialyser reuse or reprocessing can be defined as the disinfection of a dialyser for multiple uses for the same patient. Reuse requires an extensive procedure of high-level disinfection. Reused dialysers are not shared between patients. There are two ways of reusing dialysers. There is manual reuse, which involves cleaning of the used dialyser by hand and the second is the automated reuse by means of a medical device. The dialyser is automatically cleaned by machine and then filled with liquid disinfectant for storage. Automated reuse is more effective than manual reuse, but when reused over 15 times with current methodology, the dialyser can lose B2m, middle molecule clearance and fibre pore structure integrity, reducing the effectiveness of the patient dialysis session.
In Malaysia, in 2010, 90% of patients undergoing haemodialysis were using reuse dialysers and 19% of patients used their dialysers for at least 13 times. About 80% of patients were using the dialysers made from synthetic membrane. Currently, MOH haemodialysis units are using a fully automated dialyser reprocessing machine. The percentage of dialyser reuse varies according to countries. The proportion of dialysis centres that reuse dialysers in the United States had declined to 40% of dialysis centres in 2005. Japan, most of Middle East and a few scattered countries in Europe and South America do not practice any dialyser reuse.

The original reasons for introducing the dialyser reprocessing equipment in MOH Haemodialysis units were:

i. Difficulty in producing new dialysers hence the need to reuse the existing dialyser after reprocessing it

ii. The dialyser membrane is made up of 'non biocompatible' materials which incites acute inflammatory response involving complement system which result in acute and chronic adverse clinical response. After the first use, the membrane became more 'biocompatible' due to the presence of very thin lining of patients blood and protein materials on the blood sides of the membrane

iii. Cost factor whereby in the past the cost of each disposable dialyser especially the synthetic and 'high flux' types were very high

However, some of the original reasons are no longer valid. The availability of cheaper high-flux dialysers for single use means that the traditional benefit of the ability to reuse such dialysers no longer holds true. Synthetic membranes with improved blood membrane biocompatibility are now widely available, and first use syndromes have become less of an issue, particularly as ethylene oxide sterilisation is increasingly being replaced by other methods, including gamma irradiation, steam, and most recently, electron beam sterilisation.[6] The cost of reprocessing and using reprocessed dialyser is not necessary cheaper due to the rise in cost of several components required to implement dialyser reprocessing such as: the cost of staff overheads, utilities, chemicals (such as peracetic acid) and consumables, equipments (dialyser reprocessing machines, sterilant auto dilutor, dialyser auto rinser), additional physical space and facility (dedicated room for reprocessing with effective exhaust system, dialyser storage racks, clinical sinks).

The reuse of dialysers is associated with environmental contamination, allergic reactions, residual chemical infusion, inadequate concentrations of disinfectants, and pyrogens reactions. Potential errors and breakdowns in the reuse process are continuing concerns. The risk may move beyond bacteria into the realm of viruses and prions.[10] In MOH haemodialysis units, due to shortage of staffs, the dialyser reprocessing procedures are now performed by medical attendants. They are technically at risk of exposure to blood borne infections if adherence to standard precautions is not observed. It has been claimed that single use dialyser decreases rates of infection and contamination, likelihood errors and accidents, and risks associated with exposure to germicides and denatured blood products. Single use simplifies some of the operational aspects of haemodialysis and is convenient. The risk for medicolegal liability is also negligible in single use dialyser compared with reuse dialyser.[6] Therefore, there is a need to reassess the dialyser reprocessing practice in MOH haemodialysis units. This HTA was requested by the Head of Nephrology Services, Ministry of Health, Malaysia.

2. POLICY QUESTION

In MOH haemodialysis units, should single use dialyser be used for all haemodialysis patients or only for those with infectious diseases such as Hepatitis B, Hepatitis C, Hepatitis B & C co-infection or HIV infection?

3. OBJECTIVE

3.1. To assess the safety and effectiveness of single use dialyser compared with reuse dialyser for haemodialysis of patients with ESRD.

3.2. To assess the economic implications of using single use dialyser compared with resuse dialyser for haemodialysis of patients with ESRD.

3.3. To assess the environmental, legal or organizational issues related to the use of single use dialyser versus reuse dialyser.

Research questions

i. How safe is single use dialyser compared with reuse dialyser?

ii. What are the short and long term benefits of using single use dialyser compared with reuse dialyser for haemodialysis of patients with ESRD?

iii. What is the economic implication of using single use dialyser compared with reuse dialyser?

iv. What are the environmental, legal or organizational impacts of single use dialyser compared with reuse dialyser?

4. METHODS

4.1. Search Strategy

4.1.1 Electronic database will be searched for published literatures pertaining to the use of single use dialyser versus reuse dialyser.

4.1.2 Databases as follows: MEDLINE, EBM Reviews-Cochrane Database of Systematic Review, EBM-Reviews-Cochrane Central Register of Controlled Trials, EBM Reviews-Health Technology Assessment, EBM Reviews-DARE and EBM Reviews-NHS Economic Evaluation Database through the Ovid interface. Searches will also be conducted in PubMed, Horizon Scanning database, HTA database, INAHTA database, and FDA database.

4.1.3 Additional literatures will be identified from the references of the retrieved articles.

4.1.4 General search engine will also be used to get additional web-based materials and information.

4.1.5 The detail of the search strategy will be presented as appendix.

4.2. Inclusion and exclusion criteria

4.2.1. Inclusion criteria

- Study design: HTA report, Systematic Review, Randomised Controlled Trials (RCT), Non Randomised Controlled Trial, Cohort, Case-control studies, Pre and post intervention studies, Cross-sectional studies, case series and studies which include economic evaluation.
- Population: Patients with end stage renal disease on haemodialysis (adult and children).
- Intervention: Single use dialyser.
- Comparators: Reuse dialyser or reprocessed dialyser.
- Outcome:
  i. Economic (cost-analysis, cost-effectiveness)
  ii. Adverse events or complications related to the use of single use dialyser or reuse dialyser (for example infection, pyrogenic reactions, allergic reactions, first use reactions or syndromes)
  iii. Mortality risk
  iv. Survival
  v. Hospitalisation risk
  vi. Changes in membrane integrity
  vii. Legal implication
  viii. Organizational issues – operational, training
  ix. Environmental contamination
- Full text articles published in English

4.2.2 Exclusion criteria

a. Study design: Animal study, laboratory study, narrative review,
b. Non English full text article.

Based on the above inclusion and exclusion criteria, study selection will be carried out independently by two reviewers. Disagreement will be resolved by discussion.

4.3 Data extraction strategy

The following data will be extracted:

4.3.1 Details of methods and study population characteristics.

4.3.2 Details of intervention and comparators.

4.3.3 Details of individual outcomes for safety, effectiveness, cost implication, environmental, legal and organizational issues associated with the use of single use dialyser versus reuse dialyser.
Data will be extracted from selected studies by two reviewers using a pre-designed data extraction form. Disagreements will be resolved by discussion.

4.4 Quality assessment strategy

The risk of bias (methodology quality) of all retrieved literatures will be assessed using the relevant checklist of Critical Appraisal Skill Programme (CASP) by two reviewers depending on the type of the study design.

4.5 Methods of analysis/synthesis

Data on the safety, effectiveness and cost implication of using single use dialyser compared with reuse dialyser will be presented in tabulated format with narrative summaries. Meta-analysis may be conducted for this Health Technology Assessment. Local economic evaluation may be conducted.

5 Report writing

Appendix 3

SEARCH STRATEGY

Ovid MEDLINE® In-process & other Non-Indexed citations and Ovid MEDLINE® 1948 to present

1. Kidney Failure, Chronic/
2. ((chronic or end stage or end-stage) adj1 (renal failure or renal disease or kidney disease or kidney failure)).tw.
3. esrd.tw.
4. 1 or 2 or 3
5. Renal Dialysis/
6. ((renal or extracorporeal) adj1 (dialysis or dialyses)).tw.
7. h?emodialysis.tw.
8. h?emodialyses.tw.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. Kidneys, Artificial/
12. H?emodialy?er$.tw.
13. (blood adj1 dialy?er$).tw.
14. (artificial adj1 kidney$).tw.
15. single-use dialy?er$.tw.
16. dialy?er$ single-use.tw.
17. disposable dialy?er$.tw.
18. ((reuse or reprocessing) adj1 dialy?er$).tw.
19. 11 or 12 or 13 or 14 or 15 or 16 or 17
20. 11 or 12 or 13 or 14 or 18
21. 19 or 20
22. 10 and 21

Ovid- EBM Reviews- Cochrane Central Register of Controlled Trials (January 2013)

1. Kidney Failure, Chronic/
2. ((chronic or end stage or end-stage) adj1 (renal failure or renal disease or kidney disease or kidney failure)).tw.
3. esrd.tw.
4. 1 or 2 or 3
5. Renal Dialysis/
6. ((renal or extracorporeal) adj1 (dialysis or dialyses)).tw.
7. h?emodialysis.tw.
8. h?emodialyses.tw.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. Kidneys, Artificial/
12. H?emodialy?er$.tw.
13. (blood adj1 dialy?er$).tw.
14. (artificial adj1 kidney$).tw.
15. single-use dialy?er$.tw.
16. dialy?er$ single-use.tw.
17. disposable dialy?er$.tw.
18. ((reuse or reprocessing) adj1 dialy?er$).tw.
19. 11 or 12 or 13 or 14 or 15 or 16 or 17
20. 11 or 12 or 13 or 14 or 18
21. 19 or 20
22. 10 and 21

Ovid- EBM Reviews- Cochrane Database of Systematic Reviews (2005 to January 2013)

1. Kidney Failure, Chronic/
2. ((chronic or end stage or end-stage) adj1 (renal failure or renal disease or kidney disease or kidney failure)).tw.
3. esrd.tw.
4. 1 or 2 or 3
5. Renal Dialysis/
6. ((renal or extracorporeal) adj1 (dialysis or dialyses)).tw.
7. h?emodialysis.tw.
8. h?emodialyses.tw.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. Kidneys, Artificial/
12. H?emodialy?er$.tw.
13. (blood adj1 dialy?er$).tw.
14. (artificial adj1 kidney$).tw.
15. single-use dialy?er$.tw.
16. dialy?er$ single-use.tw.
17. disposable dialy?er$.tw.
18. ((reuse or reprocessing) adj1 dialy?er$).tw.
19. 11 or 12 or 13 or 14 or 15 or 16 or 17
20. 11 or 12 or 13 or 14 or 18
21. 19 or 20
22. 10 and 21

Ovid- EBM Reviews- Database of Abstracts of Review of Effects (1st Quarter 2013)

1. Kidney Failure, Chronic/
2. ((chronic or end stage or end-stage) adj1 (renal failure or renal disease or kidney disease or kidney failure)).tw.
3. esrd.tw.
4. 1 or 2 or 3
5. Renal Dialysis/
6. ((renal or extracorporeal) adj1 (dialysis or dialyses)).tw.
7. h?emodialysis.tw.
8. h?emodialyses.tw.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. Kidneys, Artificial/
12. H?emodialy?er$.tw.
13. (blood adj1 dialy?er$).tw.
14. (artificial adj1 kidney$).tw.
15. single-use dialy?er$.tw.
16. dialy?er$ single-use.tw.
17. disposable dialy?er$.tw.
18. ((reuse or reprocessing) adj1 dialy?er$).tw.
19. 11 or 12 or 13 or 14 or 15 or 16 or 17
20. 11 or 12 or 13 or 14 or 18
21. 19 or 20
22. 10 and 21

Ovid- EBM Reviews- Health Technology Assessment (1st Quarter 2013)

1. Kidney Failure, Chronic/
2. ((chronic or end stage or end-stage) adj1 (renal failure or renal disease or kidney disease or kidney failure)).tw.
3. esrd.tw.
4. 1 or 2 or 3
5. Renal Dialysis/
6. ((renal or extracorporeal) adj1 (dialysis or dialyses)).tw.
7. h?emodialysis.tw.
8. h?emodialyses.tw.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. Kidneys, Artificial/
12. H?emodialy?er$.tw.
13. (blood adj1 dialy?er$).tw.
14. (artificial adj1 kidney$).tw.
15. single-use dialy?er$.tw.
16. dialy?er$ single-use.tw.
17. disposable dialy?er$.tw.
18. ((reuse or reprocessing) adj1 dialy?er$).tw.
19. 11 or 12 or 13 or 14 or 15 or 16 or 17
20. 11 or 12 or 13 or 14 or 18
21. 19 or 20
22. 10 and 21

Ovid- EBM Reviews-NHS Economic Evaluation Database (1st Quarter 2013)

1. Kidney Failure, Chronic/
2. ((chronic or end stage or end-stage) adj1 (renal failure or renal disease or kidney disease or kidney failure)).tw.
3. esrd.tw.
4. 1 or 2 or 3
5. Renal Dialysis/
6. ((renal or extracorporeal) adj1 (dialysis or dialyses)).tw.
7. h?emodialysis.tw.
8. h?emodialyses.tw.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. Kidneys, Artificial/
12. H?emodialy?er$.tw.
13. (blood adj1 dialy?er$).tw.
14. (artificial adj1 kidney$).tw.
15. single-use dialy?er$.tw.
16. dialy?er$ single-use.tw.
17. disposable dialy?er$.tw.
18. ((reuse or reprocessing) adj1 dialy?er$).tw.
19. 11 or 12 or 13 or 14 or 15 or 16 or 17
20. 11 or 12 or 13 or 14 or 18
21. 19 or 20
22. 10 and 21

Ovid- EMBASE 1988 to 2013 Week 09

1. Kidney Failure, Chronic/
2. ((chronic or end stage or end-stage) adj1 (renal failure or renal disease or kidney disease or kidney failure)).tw.
3. esrd.tw.
4. 1 or 2 or 3
5. Renal Dialysis/
6. ((renal or extracorporeal) adj1 (dialysis or dialyses)).tw.
7. h?emodialysis.tw.
8. h?emodialyses.tw.
9. 5 or 6 or 7 or 8
10. 4 and 9
11. Kidneys, Artificial/
12. H?emodialy?er$.tw.
13. (blood adj1 dialy?er$).tw.
14. (artificial adj1 kidney$).tw.
15. single-use dialy?er$.tw.
16. dialy?er$ single-use.tw.
17. disposable dialy?er$.tw.
18. ((reuse or reprocessing) adj1 dialy?er$).tw.
19. 11 or 12 or 13 or 14 or 15 or 16 or 17
20. 11 or 12 or 13 or 14 or 18
21. 19 or 20
22. 10 and 21

Pubmed Search terms

*((((((kidney failure, chronic[MeSH Terms])) OR ((renal failure chronic) OR (chronic renal failure) OR (kidney failure chronic) OR (chronic kidney failure) OR (end stage kidney disease) OR (kidney disease end-stage) OR (renal failure end-stage) OR (end-stage renal failure) OR (end-stage renal disease) OR (renal disease end-stage) OR ersd[Title/Abstract]))) AND ((Renal dialysis[MeSH Terms]) OR ((***dialyses, renal***) OR (dialysis renal) OR (renal dialysis) OR (renal dialyses) OR (dialysis extracorporeal) OR (extracorporeal dialysis) OR (dialyses extracorporeal) OR (extracorporeal dialyses) OR (haemodialysis) OR (hemodialysis) AND title/abstract)))) AND ((((((kidneys, artificial[MeSH Terms]) OR (***hemodialyser*** *OR hemodialyser OR* ***hemodialyzer*** *OR hemodialyzer OR (blood dialyser) OR (blood dialyzer) OR (artificial kidney) OR (kidney artificial) OR (dialyzer blood) OR (***dialyser, blood***) AND title/abstract))) OR (single use dialyzers[Title/Abstract]))) OR (((((kidneys, artificial[MeSH Terms]) OR (***hemodialyser*** *OR hemodialyser OR* ***hemodialyzer*** *OR hemodialyzer OR (blood dialyser) OR (blood dialyzer) OR (artificial kidney) OR (kidney artificial) OR (dialyzer blood) OR (***dialyser, blood***) AND title/abstract))) OR (reuse dialyzers[Title/Abstract])) OR (dialyzer reuse[Title/Abstract])))*

Appendix 4

CASP CHECKLIST

SYSTEMATIC REVIEW

CRITERIA ASSESSED			
Selection of studies (relevant studies included?)	Yes ❑	No ❑	Can't tell ❑
Assessment of quality of included studies?	Yes ❑	No ❑	Can't tell ❑
If the results of the review have been combined, is it reasonable to do so? (heterogeneity)	Yes ❑	No ❑	Can't tell ❑

RCT

CRITERIA ASSESSED			
Assignment of patients randomised?	Yes ❑	No ❑	Can't tell ❑
Allocation concealment?	Yes ❑	No ❑	Can't tell ❑
Patients, health workers, study personnel blind to treatment?	Yes ❑	No ❑	Can't tell ❑
Intention to treat analysis?	Yes ❑	No ❑	Can't tell ❑
Explanation of loss to follow-up?	Yes ❑	No ❑	Can't tell ❑

COHORT

CRITERIA ASSESSED			
Selection (cohort recruited in an acceptable way?)	Yes ❑	No ❑	Can't tell ❑
Exposure accurately measured?	Yes ❑	No ❑	Can't tell ❑
Outcome accurately measured?	Yes ❑	No ❑	Can't tell ❑
Confounding factors identified and taken account?	Yes ❑	No ❑	Can't tell ❑
Follow-up of subjects complete and long enough?	Yes ❑	No ❑	Can't tell ❑

ECONOMIC EVALUATION

CRITERIA ASSESSED			
A well-define question posed?	Yes ❑	No ❑	Can't tell ❑
Comprehensive description of competing alternative given?	Yes ❑	No ❑	Can't tell ❑
Effectiveness established?	Yes ❑	No ❑	Can't tell ❑
Effects of intervention identified, measured and valued appropriately?	Yes ❑	No ❑	Can't tell ❑
All important and relevant resources required and health outcome costs for each alternative identified, measured in appropriate units and valued credibly?	Yes ❑	No ❑	Can't tell ❑
Costs and consequences adjusted for different times at which they occurred (discounting)?	Yes ❑	No ❑	Can't tell ❑
Results of the evaluation?	Yes ❑	No ❑	Can't tell ❑
Incremental analysis of the consequences and costs of alternatives performed?	Yes ❑	No ❑	Can't tell ❑
Sensitivity analysis performed?	Yes ❑	No ❑	Can't tell ❑

Appendix 5

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	1. Roth VR, Jarvis WR. Outbreaks of infection and / or pyrogenic reactions in dialysis patients. Seminars in Dialysis.2000;13(2):92-96
Study type / Methods	Cross-sectional study (summary of outbreaks investigation) From January 1980 through June 1999, the Centres for Disease control and Prevention (CDC) investigated 16 outbreaks of bacteraemia or pyrogenic reactions in haemodialysis patients.
LE	II-3
Number of patients & Patient characteristics	A total of 316 haemodialysis patients
Intervention	Single use dialyser
Comparison	Reuse dialyser
Length of follow up	
Outcome measures/ Effect size	**a. Outbreaks related to haemodialyser reuse** • **Mycobacterial infections (*Mycobacterium chelonae*) in 27 patients from one haemodialysis centre in 1982 (Bolan et al.)** ✓ **Cause:** Inadequate concentration of dialyser disinfectant (2% formaldenyde) • **Systemic non tuberculous mycobacterial infections in five high-flux dialysis patients; two deaths (Lowry et al.)** ✓ **Cause:** Inadequate concentration of dialyser disinfectant (2.5% Renalin); inadequate disinfection of water treatment system • **Gram-negative Bacteraemia and pyrogenic reactions in six patients (CDC, unpublished)** ✓ **Cause:** Dialyser disinfectant diluted to improper concentration (2.5% Renalin) • **Gram-negative Bacteraemia in six patient (CDC, unpublished)** ✓ **Cause:** Dialyser disinfectant diluted to improper concentration; water for reuse did not meet Advancement of Medical Instrumentation (AAMI) standards • **Nine pyrogenic reactions and five gram-negative bacteraemia in 11 patients (Beck et al.)** ✓ **Cause:** Inadequate mixing of dialyser disinfectant (Renalin) • **Gram-negative bacteraemia in 33 patients in six haemodialysis centres (Murphy, CDC)** ✓ **Cause:** Dialyser disinfectant (chlorine dioxide-based disinfectant) altered the dialyser membrane integrity causing leaks in the membrane • **Bacteraemia in six patients (*Klebsiella pneumonia*) in 1992: all blood isolates had similar plasmid profiles (Welbel et al.)** ✓ **Cause:** Dialyser contaminated during removal and cleaning of headers with gauze; staff not routinely changing gloves; dialysers not processed for several hours after disassembly and cleaning • **Pyrogenic reactions in three high-flux dialysis patients (CDC,unpublished)** ✓ **Cause:** Dialyser reprocessed with two disinfectants (4% formaldehyde and 2.5% Renalin) was taught to impair membrane integrity; water for reuse did not meet AAMI standards

Outcome measures/ Effect size (cont...)	**b. Outbreaks related to inadequate water treatment** • **Pyrogenic reactions in six patients; seven bacteraemias (Jackson et al.)** ✓ **Cause:** Inadequate disinfection of water distribution system and dialysis machines; improper microbial assay procedure • **Mycosystin-induced acute liver failure in 101 of 124 haemodialysis patients in Caruara, Brazil patient in 1996; 50 deaths (Jechimsen et al.)** ✓ **Cause:** Inadequate water treatment at municipal plant and dialysis centre (mycrocystins produced by cyanobacteria were detected in water from the reservoir and from dialysis centre and in serum and liver tissue of case patients) **c. Outbreaks related to contaminated dialysis fluid** • **13 pyrogenic reactions in 10 high-flux dialysis patients; 1 death (CDC, unpublished)** ✓ **Cause:** Inadequate concentration of dialyser disinfectant; dialyzers rinsed with city water; water for reuse did not meet AAMI standards • **18 pyrogenic reactions in 16 patients in 1987 (Gordon et al.)** ✓ **Cause:** Dialysers rinsed with city water containing high levels of endotoxin; water for reuse did not meet AAMI standards. *Pseudomonas* and *Enterobacter* species were recovered from the dialysate. • **Pyrogenic reactions in 22 patients (Rudnick et al.)** ✓ **Cause:** Water for reuse did not meet AAMI standards; improper microbial assay technique. **d. Outbreaks related to contaminated dialysis machine** • **Three pyrogenic reactions and 10 bacteremias in patients treated on machines with a port for disposal of dialyser priming fluid [waste handling option (WHO)] in 1996 (Jochimsen et al.)** ✓ **Cause:** Incompetent valve allowing backflow from drain to the WHO; bacterial contamination of the WHO • **Bacteremias in 10 patients treated on machines with (WHO)] in 1996 (Wang et al.)** ✓ **Cause:** Incompetent valve allowing backflow from drain to the WHO; bacterial contamination of the WHO **e. Outbreaks related to central vein catheters** • **Bacteremias in 35 patients with central vein catheters (CDC, unpublished)** ✓ **Cause:** Central vein catheters used as primary access; median duration of infected catheters was 311 days; improper aseptic techniques **Summary** The dialysis-related outbreaks demonstrate the on-going potential for infection-related morbidity and mortality among dialysis patients. Many of these outbreaks could have been prevented by adequate water treatment, proper disinfection of water systems and dialysis machines, adherence to recommended reprocessing protocols for centres reusing dialysers, and more stringent quality control monitoring.
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	2. Vanholder R, Vanhaecke E, Ringoir S. Waterborne pseudomonas Septicaemia. ASAIO Transactions.1990;36:M215-M216
Study type / Methods	Case series in Belgium.
LE	II-3
Number of patients & Patient characteristics	Three patients in a dialysis unit.
Intervention	Single use dialyser
Comparison	Reuse dialyser • Dialyser disinfectant (formaldehyde)
Length of follow up	
Outcome measures/ Effect size	**Septicaemia with *Pesudomonas species*** • *Pseodomonas aeruginosa*, *P. Maltophilia*, and / or *P. Vesicularis* were found in the blood cultures of three patients in whom four pyrogenic reactions developed. *Pesudomonas* were also cultured from the effluent of two dialysers reprocessed with formaldehyde and not yet use; these two dialysers had extremely low formaldehyde concentrations. The tap water used for dialyser rinsing in the reuse procedure contained only 220 colony forming units/ ml pseudomonas. The problem appeared to be related to the inadequate mixing of the sterilant with the tap water used in the automated reprocessing device.
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	3. Powe NR, Jaar B, Furth SL, Hermann J, Briggs W. Septicemia in dialysis patients: incidence, risk factors and prognosis. Kidney International.1999;55(3):1081-1090
Study type / Methods	Cohort study The objective of the study was to identify patients at high risk and to characterise modifiable risk factors for septicaemia in patients with ESRD. Conducted a longitudinal cohort study of incident ESRD patients in the case-mix study of the U.S. Renal Data System with seven years of follow-up from hospitalisation and deaths records. Poisson regression was used to examine independent risk factors for hospital-managed septicaemia. Cox proportional hazards analysis was used to assess the independent effect of septicaemia on all-cause mortality and on death from septicaemia. Separate analyses were performed for patients on peritoneal dialysis (PD) and haemodialysis (HD). Baseline data from a special case-mix study of the U.S. renal data System (USRDS) and follow-up data from hospitalisation and death records in the USRDS. Patients were randomly selected from the national population of the ESRD patients in the Medicare ESRD registry using two stage cluster sampling procedure. The criteria for selection were initiation of chronic maintenance dialysis for ESRD in 1986 or 1987, Medicare entitlement for dialysis services, no transplantation as initial renal replacement therapy, and treatment at dialysis facility that was within one day of travel of the ESRD network office.
LE	II-2
Number of patients & Patient characteristics	A total of 4,005 haemodialysis patients • Age: (Mean ±SD) = 60.0 (15.9) years • 47.7% females • 39.2% black race • 40.0% diabetes mellitus • 57.0% reuse dialysers
Intervention	Single use dialyser
Comparison	Reuse dialyser
Length of follow up	7 years

Outcome measures/ Effect size	**a. Episodes of septicaemia (admission to hospital for septicaemia)** • 11.7% of haemodialysis patients had at least one episode of septicaemia that was managed in the hospital • **Potential sources of infection** ✓ Infection/inflammation caused by internal prostheses ✓ Vascular access infection, other complications of internal prosthetic device ✓ Decubitus ulcer, Urinary tract infection, pneumonia, gangrene, endocarditis, cellulitis and abscess of the foot • Age > 65 years ✓ [Adjusted risk ratio (95% CI) = 1.75 (1.48 to 2.06)] • Diabetes Mellitus ✓ [Adjusted risk ratio (95% CI) = 1.26 (1.06 to 1.50)] • Serum albumin < 3.5 g/dl ✓ [Adjusted risk ratio (95% CI) = 1.66 (1.38 to 1.99)] • **Reuse of dialysis membranes (entire follow-up period, up to 7 years)** ✓ **[Adjusted risk ratio (95% CI) = 1.28 (1.05 to 1.56)]** **b. Association of septicaemia with death** • Death from all causes ✓ [Adjusted risk ratio (95% CI) = 2.40 (2.12 to 2.72)] • **Death from septicaemia** ✓ **[Adjusted risk ratio (95% CI) = 9.79 (6.49 to 14.76)** • Death from other causes ✓ [Adjusted risk ratio (95% CI) = 2.14 (1.87 to 2.45) **Authors conclusion** Septicaemia, which carries a marked increased risk of death, occurs frequently in patients on peritoneal dialysis as well as haemodialysis. Early referral to a nephrologist, improving nutrition, and avoiding temporary vascular access may decrease the incidence of septicaemia.
General comments	Quality assessment (CASP) 1. Yes 2. Yes 3. Yes 4. Yes 5. Can't tell (not mentioned about blinding) 6. Yes 7. Yes 8. Risk ratio, 95% CI 9. CI is not wide

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	4. Tokars JI, Alter MJ, Favero MS, Moyer LA, Miller E, Bland LA. National surveillance of dialysis-associated diseases in the United States-1992.ASAIO Journal.1994;40:1020-1031
Study type / Methods	Cross-sectional study in the United States in 1992 (yearly survey). The objectives were to determine (A) the frequency with which certain haemodialysis practices, including measures designed to prevent disease, are used; (B) to determine the frequency of hemodialysis-associated complications and diseases; and (C) to use this information to suggest further measures to prevent complications and disease in haemodialysis patients and staffs. In conjunction with the annual facility survey by the Health Care Financing Administration HCFA) for calendar year 1992, Centre for Disease Control and Prevention (CDC) distributed a questionnaire by mail to all 2,321 chronic haemodialysis centres licensed by HCFA.
LE	II-3
Number of patients & Patient characteristics	• Number of centres = 2,170 • Number of patients = 170,028 • Number of staffs = 43,535
Intervention	Single use dialyser
Comparison	Reuse dialyser • Number of haemodialysis centres having dialyzer reuse programmes =1,569 (72%) • 50% used high flux dialyser membrane, 50 conventional dialyser membranes • Germicides used: - Formaldehyde (40%) - Peracetic acid (52%) - Glutaraldehyde (8%)
Length of follow up	
Outcome measures/ Effect size	• **Effect of separation practices for HBsAg positive patients on incidence of HBsAg in haemodialysis patients** **Incidence of HBsAg (%) by separation practices:** ✓ Room and machine = 0.2, P < 0.05 versus machine only and none ✓ Machine only = 0.4 ✓ None = 0.3 • **Single use versus reuse:** ✓ Reuse of dialysers was not associated with increased risk of HBV infection in either patients or staffs (data not shown) ✓ Anti-HCV prevalence among staffs = 1.6% in reused versus 1.5% not reuse (similar) • **Pyrogenic reactions (PR):** ✓ 19% of centres reporting pyrogenic reactions in the absence of septicaemia ❖ Single use = 13, reuse 22, P < 0.05 ❖ High flux dialyser membrane; none = 14, any = 25, P < 0.05 ❖ High flux dialysis; none= 15, any = 28, P < 0.05 • **New Dialyser Syndrome:** ✓ Reported in patients by 24% of centres. ✓ Reuse versus single use (27% versus 17%, OR = 1.6, P < 0.001) ✓ Reported most frequently by centres using regenerated cellulose (P < 0.001) and cuprophan membranes (P < 0. 001)
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	5. Tokars JI, Alter MJ, Miller E, Moyer LA, Favero MS. National surveillance of dialysis-associated diseases in the United States-1994.ASAIO Journal.1997;43:108-119
Study type / Methods	Cross- sectional study in the United States in 1994 (yearly survey). The objectives were to determine (A) the frequency with which certain haemodialysis practices, including measures designed to prevent disease, are used; (B) to determine the frequency of hemodialysis-associated complications and diseases; and (C) to use this information to suggest further measures to prevent complications and disease in haemodialysis patients and staffs. In conjunction with the annual facility survey by the Health Care Financing Administration HCFA) for calendar year 1994, Centre for Disease Control and Prevention (CDC) distributed a questionnaire by mail to all 2,625 chronic haemodialysis centres licensed by HCFA.
LE	II-3
Number of patients & Patient characteristics	• Number of centres = 2,449 • Number of patients = 206,884 • Number of staffs = 50,314
Intervention	Single use dialyser
Comparison	Reuse dialyser • Number of haemodialysis centres having dialyzer reuse programmes =1,835 (75%) • 45% used high flux dialysis • Germicides used: - Formaldehyde (40%) - Peracetic acid (52%) - Glutaraldehyde (7%) - Heat (1%) Mean average reuse =15
Length of follow up	
Outcome measures/ Effect size	• **Effect of separation practices for HBsAg positive patients on incidence of HBsAg in haemodialysis patients** **Incidence of HBsAg (%) by separation practices:** ✓ Neither room nor machine= 0.12 ✓ Room only = 0.06 ✓ Machine only = 0.14 ✓ Room and machine = 0.11 ✓ Do not treat = 0.06 (Ref) • **Single use versus reuse:** ✓ Reuse of dialysers was not associated with increased risk of HBV infection in either patients or staffs (data not shown) ✓ Anti-HCV prevalence among staffs = 1.8% in reused versus 2.0% not reuse (similar) • **Pyrogenic reactions (PR):** ✓ 22% of centres reporting pyrogenic reactions in the absence of septicaemia ❖ Single use = 14, reuse 24, P < 0.05 ❖ High flux dialyser membrane; none =17, any = 24, P < 0.05 ❖ High flux dialysis; none = 18, any = 26, P < 0.05 • **New Dialyser Syndrome:** ✓ Reported in patients by 28% of centres. ✓ Reuse versus single use (30% versus 21%, OR=1.5, P = 0.0009) ✓ Reported most frequently by centres using regenerated cellulose (P = 0.001) and cuprophan membranes (P < 0. 001)
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	6. Tokars JI, Miller E, Alter MJ, Arduino MJ. National surveillance of dialysis-associated diseases in the United States, 1995.ASAIO Journal.1998;44:98-107
Study type / Methods	Cross-sectional study in the United States in 1995 (yearly survey). The objectives were to determine (A) the frequency with which certain haemodialysis practices, including measures designed to prevent disease, are used; (B) to determine the frequency of hemodialysis-associated complications and diseases; and (C) to use this information to suggest further measures to prevent complications and disease in haemodialysis patients and staffs. In conjunction with the annual facility survey by the Health Care Financing Administration HCFA) for calendar year 1995, Centre for Disease Control and Prevention (CDC) distributed a questionnaire by mail to all 2,762 chronic haemodialysis centres licensed by HCFA.
LE	II-3
Number of patients & Patient characteristics	• Number of centres = 2,647 • Number of patients = 224,954 • Number of staffs = 54,194
Intervention	Single use dialyser
Comparison	Reuse dialyser • Number of haemodialysis centres having dialyzer reuse programmes =2,048 (77%) • Germicides used: - Formaldehyde (38%) - Peracetic acid (54%) - Glutaraldehyde (7%) - Heat (1%) Mean average reuse =15
Length of follow up	
Outcome measures/ Effect size	• **Effect of separation practices for HBsAg positive patients on incidence of HBsAg in haemodialysis patients** **Incidence of HBsAg (%) by separation practices:** ✓ Room, machine and staff = 0.06 ✓ Room and machine but not staff = 0.06 ✓ Do not treat = 0.05 • **Single use versus reuse:** ✓ Reuse of dialysers was not associated with increased risk of HBV infection in either patients or staffs (data not shown) ✓ Anti-HCV prevalence among staffs = 1.9% in reused versus 2.1% not reuse (similar) • **Pyrogenic reactions (PR):** ✓ 20% of centres reporting pyrogenic reactions in the absence of septicaemia ❖ Single use = 13, reuse 22, P < 0.05 ❖ High flux dialyser membrane; none = 16, any =21, P < 0.05 ❖ High flux dialysis; none=16, any = 23, P < 0.05 (reuse of dialysers , used of high flux dialyser membrane and the use of high flux dialysis were associated with increased reporting of pyrogenic reactions) • **New Dialyser Syndrome:** ✓ Reported in patients by 23.5% of centres.
General comments	

Evidence Table : Safety

Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	7. Tokars JI, Miller E, Alter MJ, Arduino MJ. National surveillance of dialysis-associated diseases in the United States, 1997.Seminars in Dialysis.2000;13(2):75-85
Study type / Methods	Cross- sectional study in the United States, 1997 (yearly survey). The objectives were to determine (A) the frequency with which certain haemodialysis practices, including measures designed to prevent disease, are used; (B) to determine the frequency of hemodialysis-associated complications and diseases; and (C) to use this information to suggest further measures to prevent complications and disease in haemodialysis patients and staffs. In conjunction with the annual facility survey by the Health Care Financing Administration HCFA) for calendar year 1997, Centre for Disease Control and Prevention (CDC) distributed a questionnaire by mail to all 3,228 chronic haemodialysis centres licensed by HCFA.
LE	II-3
Number of patients & Patient characteristics	• Number of centres = 3,077 • Number of patients = 253,001 • Number of staffs = 63,054
Intervention	Single use dialyser
Comparison	Reuse dialyser • Number of haemodialysis centres having dialyzer reuse programmes =2,523 (82%) • Germicides used: - Formaldehyde (34%) - Peracetic acid (56%) - Glutaraldehyde (7%) - Heat (3%) Mean average reuse =17
Length of follow up	
Outcome measures/ Effect size	• **Effect of separation practices for HBsAg positive patients on incidence of HBsAg in haemodialysis patients** **Incidence of HBsAg (%) by separation practices:** ✓ Room and machine = 0.055 ✓ Machine only = 0.038 ✓ None = 0.037 ✓ No difference HBV incidence in centres where separate staff members were used to treat HBsAg-positive patients • **Single use versus reuse:** ✓ Reuse of dialysers was not associated with increased risk of HBV infection in either patients or staffs (data not shown) ✓ Anti-HCV prevalence among staffs = 1.6% in reused versus 1.7% not reuse (similar) • **Pyrogenic reactions:** ✓ 21% of centres reporting pyrogenic reactions in the absence of septicaemia • **New Dialyser Syndrome:** ✓ Reported in patients by 23% of centres. Proportion reporting this complication has decreased from 43% of centres in 1984
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	8. Favero MS, Deane N, Leger RT, Sosin AE. Effect of Multiple use of dialyzers on hepatitis B incidence in patients and staff. JAMA.1981;245(2):166-167
Study type / Methods	Cross- sectional study in the United States. The objective was to assess whether the practice of reuse of dialysers placed staff members and patients at an increased risk of acquiring infection. Data pertaining to incidence of hepatitis B from a 1976 Centre for Disease Control Study were matched with responses from a renal Physicians Association survey on dialyser reuse in the United States.
LE	II-3
Number of patients & Patient characteristics	• 6,079 haemodialysis patients in 96 centres practising reuse dialysers • 18,847 haemodialysis patients in 413 centres where single use was practised • 3,049 staffs in 96 centres practising reuse dialysers • 8,696 staffs in 413 centres where single use was practised
Intervention	Single use dialyser
Comparison	Reuse dialyser
Length of follow up	
Outcome measures/ Effect size	**Hepatitis B surface antigen (HBsAg) positive** • **Patients (reuse versus single use):** Reuse = 166/6,079 (2.7%) Single use = 495/18,947 (2.6%) • **Staffs (reuse versus single use):** Reuse = 75/3,049 (2.5%) Single use = 200/8,696 (2.3%) • Incidence of infection among staff associated with a centre having at least one HBsAg-positive patients was 2.9% in centres practicing reuse versus 3.6% in centres practicing single use • Nearly 95% staff who became HBsAg-positive were associated with centres having at least one HBsAg-positive patient **Authors conclusion** The practice of reusing dialysers does not appear to be associated with increased risk of hepatitis B infection among patients and staffs
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	9. Centers for Disease Control and Prevention: Outbreaks of hepatitis B virus infection among hemodialysis patients -California, Nebraska, and Texas,1994.MMWR.45(14):285-289, 1996. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/00040762.htm. Accessed on 22/3/2013
Study type / Methods	Case series From April through August 1994, outbreaks of hepatitis B virus (HBV) infection occurred in five chronic haemodialysis centres in California, Nebraska and Texas. Investigations were conducted by state and local public health officials and CDC.
LE	II-3
Number of patients & Patient characteristics	• Haemodialysis Centre A, Texas ✓ Acute HBV infection in 14 of 20 patients (70%) • Haemodialysis Centre B, California ✓ Acute HBV infection in 7 of 131 patients (5.3%) • Haemodialysis Centre C, California ✓ 4 of 42 patients (9.5%) • Haemodialysis Centre D, California ✓ 11 of 77 patients (14%) • Haemodialysis Centre E, Nebraska ✓ 2 of 303 patients (0.7%)
Intervention	Haemodialysis
Comparison	
Length of follow up	
Outcome measures/ Effect size	**Causes of outbreak** • Transmission of HBV from haemodialysis patients with chronic HBV infection to susceptible patients resulted from failure to identify and isolate HBV-infected patients during haemodialysis, sharing of staff, equipment, and supplies among patients; and failure to vaccinate susceptible patients against hepatitis B.
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	10. Pinto dos Santos J, Loureiro A, Neto Cendoroglo Neto M, Pereira BJG. Impact of dialysis room and reuse strategies on the incidence of hepatitis C virus infection in haemodialysis units.Nephrol Dial transplant.1996;11:2017-2022
Study type / Methods	Cross- sectional study in Portugal in 1994. The objective was to analyse trends in the prevalence and incidence of HCV infection, and evaluate the impact of dialysis room and reuse policies on the incidence of HCV infection. A hospital survey instrument was sent out to medical directors of all 71 haemodialysis (HD) units in Portugal in August 1994. Information for the years 1991, 1992 and 1993 was requested with respect to HCV infection, defined as positive anti-HCV test. Sixty-two of 71 units (87%) treating 4,232 patients in 1993 responded. Overall, data from 5,774 patient-years were available for analyses. By 1993, regular anti-HCV testing of patients and staff was practised by 98% and 82% of units respectively.
LE	II-3
Number of patients & Patient characteristics	• Number of centres = 62 • Number of patients = 4,232 patients
Intervention	Single use dialyser
Comparison	Reuse dialyser
Length of follow up	
Outcome measures/ Effect size	**Incidence of anti-HCV inflection** • Decline in incidence from 909% in 1991 to 5.7% in 1992 and 5.1% in 1993 • Wide variation in the incidence of HVC infection in HD across the country: **Lowest among unit that:** ✓ Located in northern region ✓ Private hospital based units • **Impact of dialysis room strategies on the incidence of HCV infection** ✓ No policy:(Odds Ratio=1) ✓ Used dedicated machines/ stations for all patients:- - (Odds Ratio, 95% CI) = 1.46(1.14 to 1.86), P = 03003 ✓ Used dedicated machines/ stations for HCV-Positive patients:- - (Odds Ratio, 95% CI) = 0.22 (0.11 to 0.43), P <0.001 ✓ Used separate room for HCV-positive patients:- - (Odds Ratio, 95% CI) = 0.46 (0.29 to 0.73), P = 0.001 ✓ Used separatearea for HCV-position patients:- - (Odds Ratio, 95% CI) = 1.00 (0.73 to 1.35), P = 0.98 • **Impact of reprossing dialysers on the incidence of HCV infection:** ✓ Not reprocessed :- - (Odds Ratio, 95% CI) = 1.00 • **Reprocessed** - (Odds Ratio, 95% CI) = 0.82 (0.64 to 1.04), P = 0 • **Impact of dialyser reprocessing strategies for dialyser from anti-HCV-positive patients on the incidence of HCV infection in haemodialysis units that reprocessed dialysers:** ✓ No policy:- - (Odds Ratio, 95% CI) = 1.0 ✓ Reprocessed last:- - (Odds Ratio, 95% CI) = 1.53 (1.07 to 2.18), P = 0.02 ✓ Separate equipment :- - (Odds Ratio, 95% CI) = 1.03 (0.77 to 1.38), P = 0.86 ✓ Separate room:- - (Odds Ratio, 95% CI) = 1.03 (0.77 to 1.38), P = 0.86 ✓ Not reprocessed (ban on reuse of dialysers):- - (Odds Ratio, 95% CI) = 0.27 (0.13 to 0.59), P < 0.001 • **Renalin versus formaldehyde:-** ✓ Odds Ratio, 95% CI) = 0.62 (0.46 to 0.84), P = 0.002 **Authors conclusion** The results suggest the transmission of HCV infection in HD units and that the use of dedicated machines and isolation of anti-HCV-positive patients and their dialysers may reduce the incidence of HCV infection.
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	11. Key J, Nahmias M, Acchiardo S. Hypersensitivity reaction on first-time exposure to Cuprophan hollow fiber dialyzer. American Journal of Kidney Diseases.1983;119(6):664-666
Study type / Methods	Case series in the US. Forty-five patients who have been maintained on haemodialysis using a regenerated cellulose hollow fibre artificial kidney [HFAK (Cordis Dow C-DAk 1.3m²/1.8 m²)] were dialysed on cuprophan HEAK (Travenol laboratories CF-1200,1500) for the first time. All dialysers were prepared for use following the manufacturer's recommended set-up and priming procedure.
LE	II-3
Number of patients & Patient characteristics	3 of 45 patients (6.6%). Case 1 A 44 year- old black male with chronic renal failure has been on chronic haemodialysis three times/week for 3.5 hours for 88 months. Case 2 A 52 year-old black female with diagnosis of diabetic nephropathy has been maintained on chronic haemodialysis three times per week for 30 months. Case 3 A 61 year- old black female with nephrosclerosis has been on dialysis twice a week, for 4 hours a session, for 50 months.
Intervention	Cuprophan hollow fibre dialyser
Comparison	-
Length of follow up	
Outcome measures/ Effect size	**Hypersensitivity reaction on first time exposure to Cuprophan hollow fibre dialyser** • Within seconds in one patient and within 10-16 minutes in two patients, respiratory distress, urticaria, pruritus, hypertension/hypotension, and facial oedema developed. • They were treated with oxygen, epinephrine, and diphenhydramine. Two patients received an intermittent positive pressure breathing treatments and one received IV methyl-prednisolone. • After allowing 10-15 minutes for stabilisation, the dialysis was resumed on a non-cuprophan hollow fibre artificial kidney (regenerated cellulose hollow fibre dialyser). Patients were discharged with no sequelae. • The cause of the hypersensitivity reaction is unknown.
General comments	

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	12. Pegues DA, Beck-sague CM, Wollen ST, Greenspan B, Burns SM, Bland LA, Arduino MJ, Favero MS, Mackow RC, Jarvis WR. Anaphylactoid reactions associated with resue of hollow-fiber hemodialyzers and ACE inhibitors. Kidney International.1992;42:1232-1237
Study type / Methods	Cohort study at a haemodialysis centre in Virginia in 1989. The objective was to indentify the risk factors for anaphylactoid reactions (AR). The study was conducted by CDC, FDA and Virginia State Department of Health. Case findings was performed by reviewing medical records including dialysis treatment records, for all patients receiving haemodialysis at Continental Dialysis Centre of Springfiled-Fairfax (CD-SF) from January 1 through November 27 1989. To identify risk factors for ARs, they performed a cohort study of all patients receiving dialysis treatments on the six days when the reactions occurred.
LE	II-2
Number of patients & Patient characteristics	• 12 cases of AR occurred in ten patients with chronic renal failure, one patient had three ARs. • 48 patients receive haemodialysis treatment in the centre. • 44 patients received 101 dialysis treatments on the six days of the study period when patients experienced ARs.
Intervention	First use dialyser
Comparison	Reuse dialyser • Dialyser type: ✓ Conventional hollow –fibre dialysers with cellulose acetate or Cuprophan membrane ✓ High flux using polysulfone hollow-fibre dialysers • Germicide used for reprocessing; ✓ 3.3% Renalin (peracetic acid / hydrogen peroxide) • Automated reprocessing machine
Length of follow up	
Outcome measures/ Effect size	**Anaphylactoid reactions (AR)** (From July 18 through November 27, 1989) • 12 ARs occurred in 10 patients, one patient required hospitalisation, no patients died ✓ ARs occurred within minutes of initiating dialysis and were characterised by peripheral numbness and tingling, laryngeal oedema or angiooedema, facial or generalised sensation of warmth, and / or nausea or vomiting • All 12 ARs occurred with dialysers that had been reprocessed with an automated reprocessing system • Exposed to reused dialysers versus new dialysers:- ✓ 12/70 sessions versus 0/31 sessions; RR undefined; P = 0.016 • Treated with angiotension-converting enzyme (ACE) inhibitor versus not treated:- ✓ 7/10 versus 3/33; RR = 7.9; 95% CI = 2.5 to 25.2 • Mean number of haemodialyser reuses (case-sessions versus non-case sessions):- ✓ 10.3 versus 6.2; P = 0.016 • After reuse of dialysers was discontinued at the centre, no further ARs occurred, despite continued administration of ACE inhibitors. **Authors conclusion** We hypothesise that the interaction between dialyser that has been repeatedly reprocessed and reused, blood and additional factors, such as ACE inhibitors, increased the risk of developing ARs.
General comments	Quality assessment (CASP) 1. Yes 2. Yes 3. Yes 4. Yes 5. Can't tell (not mentioned about blinding) 6. Can't tell 7. Yes 8. RR, 95% CI, P value

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	13. Pereira BJG, Batov SN, Sundararm S, Schmid CH, Trabeisi FR, Strom JA, King AJ. Impact of single use versus reuse of cellulose dialyzers on clinical parameters and indices of biocompability. J Am Soc Nephrol.1996;7:861-870
Study type / Methods	Randomised controlled trial at the outpatient dialysis unit at St. Elizabeth's Medical Centre, Boston. Objective of the study was to compare the qualitative and/or quantitative differences in activation of cellular and plasma elements, intradialytic signs and symptoms, adequacy of dialysis, and serum biochemistry and haematology in patients dialysed with new or reprocessed cellulose dialysers. The study measured the plasma levels and production of interleukin-1 receptor antagonist (IL-1Ra) by peripheral blood monocular cells (PBMC), indices of cytokine synthesis; plasma C3a levels, an index of complement activation; plasma levels of polysaccharide binding protein (LBP), an acute phase reactant; and plasma levels of bactericidal-permeability increasing factor (BPI), a neutrophil primary granule protein. The indices were studies before dialysis, 15 minutes after start of dialysis, and at the conclusion of dialysis in both groups.
LE	II-2
Number of patients & Patient characteristics	39 patients;-. • 20 patients assigned to reuse dialysers completed the study • 17 patients assigned to single use dialysers completed the study
Intervention	Single use cellulose membrane dialyser • Low flux
Comparison	Reuse cellulose membrane dialyser • Low flux • Dialysers processed with sodium hypochlorite (< 1%) and disinfection with gluteraldehyde (0.8%) using an automated system. Mean number of reuses = 7 ± 1
Length of follow up	12 weeks
Outcome measures/ Effect size	**a. Clinical and laboratory characteristics during 12 week study period (single use versus reuse)** • Hospital admission days: ✓ Single use 1 ± 1: reuse 1 ± 0, P = 0.32 • No episodes of chills or rigors or fever in both groups • Episodes of symptomatic hypotension: ✓ Single use 8 ± 2: reuse 11 ± 3, P = 0.75 • Mean monthly urea reduction ratio (%): ✓ Single use 65 ± 2: reuse 63 ± 2, P = 0.36 **b. At the completion of the 12 week study (single use versus reuse)** • No significant difference in haematocrit, white cell count, serum calcium, serum phosphorus, serum cholesterol, serum triglycerides, serum total protein and serum albumin between the two groups. **Authors conclusion** These results suggest that the reprocessing of cellulose dialysers with gluteraldehyde and bleach does not affect indices of biocompatibility, intradialytic symptoms and signs, adequacy of dialysis, or serum biochemistry and haematology**.**
General comments	Quality assessment (CASP) 1. Yes 2. Can't tell (not mentioned method of randomisation) 3. Yes 4. Yes 5. Yes 6. Yes 7. Number and P value

Evidence Table : Safety
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Bibliographic citation	14. Churchill DN, Taylor DW, Shimizu AG, Beecroft ML, Singer J, Barnes CC, Ludwin D, Wright N, Sackett DL, Smith EKM. A Multiple crossover study with random allocation to order of treatment. Nephron.1988;50: 325-331
Study type / Methods	Multiple crossover design with random allocation to order consisting of six 10-week crossover periods conducted in St Joseph's Hospital, Hamilton, Ontario, Canada. Aim of the study was to evaluate the effect of dialyser reuse on fever, blood leaks, serum urea and creatinine values and symptoms. Each of 6 crossover periods consisted of 4 weeks on either single use or reuse, 1 week washout, 4 weeks on the alternative treatment and 1 week washout. The reuse consisted of six uses of each dialyser and the washout weeks consisted of three single use sessions.
LE	II-2
Number of patients & Patient characteristics	51 patients • 31 males (60.8% males) • 20 females (39.2%) • Mean age ; 58.7 years for males and 56.2 years for females 49 patients completed at least one crossover period 32 patients completed all 6 crossover periods
Intervention	Single use dialyser • All subjects used hollow-fibre dialysers; 42 cuprophane, 9 cellulose acetate
Comparison	Reuse dialyser • Dialysers reprocessed with formaldehyde • Mean number of reuses was 4.4 for cuprophane hollow-fibre dialysers and 3.8 for cellulose acetate hollow-fibre dialysers
Length of follow up	Six 10-week period
Outcome measures/ Effect size	• 49 patients completed at least one crossover period, 32 patients completed all 6 crossover periods. Reasons for 17 non completion of 6 crossover period: ✓ 5 deaths, 1 transplant, 2 transfers to home dialysis, 2 changed in dialysis prescription, (withdrawals -3 patients request, 2 physician request), 2 late entry • Mean temperature change (°C): post-minus predialysis: ✓ Reuse minus single use: Mean (SEM) = 0.008°C (0.208) • Blood leaks: ✓ 2 during 2,590 single use dialysis session ✓ 1 during 2,590 reuse dialysis session • Mean serum urea values (mmol/l) before first dialysis of washout week: ✓ Reuse minus single use: Mean (SEM) = 0.25 (0.41) • Mean serum creatinine values (umol/l) before first dialysis of washout week: ✓ Resuse minus single use: Mean (SEM) = 1 (10) • There was no differences for symptoms of pruritis, cramps, nausea, headache, chest pain, backache or fatique between reuse and single use dialysers **Authors conclusion** There were no clinical advantages or disadvantages associated with dialyser reuse.
General comments	Quality assessment (CASP) 1. Yes 2. Can't tell (not mentioned method of randomisation) 3. Yes 4. Yes 5. Not relevant 6. Yes 7. Mean (SEM)

Evidence Table : Safety
Question : Is single use dialyser safer compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis?

Bibliographic citation	15. Kant KS, Pollak VE, Cathey M, Goetz D, Berlin R. Multiple use of dialyzers: safety and efficacy. Kidney Int.1981;19 (5):728-738
Study type / Methods	Comparative study in Dialysis Clinic-Cincinnati, a 'free-standing" dialysis unit from July 1978 to 30 September 1979. The practice of multiple use of dialysers was examined over a 15-month period on all 104 patients in chronic maintenance haemodialysis facility. A computerised medical information system permitted analysis of the incidence of events in over 10,000 successive haemodialysis. It also allowed analysis of events in 27 patients dialysed for a total of 655 months successfully in two units practicing single and multiple dialyser reuse. Three types of dialyser were used – C-DAK 1.3 m^2, C-DAK 1.8 m^2, C-DAK 3500 (manufactured by Cordis Dow)
LE	II-3
Number of patients & Patient characteristics	104 patients;-. • 44 males (42.3% males) • 18 had diabetes mellitus • Sub-analysis in 27 patients dialysed at the unit practicing reuse in the free standing dialysis centre (DCC) for a period of 334 patient months and dialysed previously in a unit that did not practice reuse (UCMC) for a comparable earlier period totalling 321 months.
Intervention	Single use dialyser
Comparison	Reuse dialyser • Dialysers reprocessed with 1.5% formaldehyde • Average 7.40 uses per dialyser
Length of follow up	15 months
Outcome measures/ Effect size	**Incidence of selected findings occurring during haemodialysis in 27 patients dialysed for a comparable period of times in two facilities (using dialyser once versus reusing dialyser)** • Associated with infection: ✓ Fever, sweating, respiratory distress, chest pain, tenderness over fistula/graft (significantly lower in reuse dialyser) ✓ Chills, discharge or infection of fistula / graft (no significant difference) • Presumably not associated with infection: ✓ Hypotension, nausea/vomiting (significantly lower in reuse, P <0.001) ✓ Cramps (no significant difference) • In facility practicing reuse, the incidence of fever, chills, and sweating was the same when the dialyser was used for the first time or was reused (P>0.3) • Rate of hospitalisation (no significant difference when treated in facility practising reuse or single use) **Authors conclusion** Multiple dialyser use over a 15-month period is safe, efficacious, and not associated with an increased rate of infection, morbidity from any cause or mortality**.**
General comments	

Evidence Table : Membrane integrity
Question : Does reuse of dialyser affect dialyser performance?

Bibliographic citation	1. Cheung AK, Agodoa LY, Daugirdas JT, Depner TA, Cotch FA, Greene T, Levin NW, Leypoldt JK, The Hemodialysis (HEMO) Study Group. Effects of hemodialyzer reuse on clearances of urea and β_2-Microglobulin. J Am Soc Nephrol.1999;10:117-127
Study type / Methods	Randomised multicentre trial sponsored by the U.S. National Institute of Health. The present study analyses data extracted from a multicentre clinical trial (15 clinical centres with more than 45 dialysis units) and examines the effects of reuse on urea and β_2-microglobulin (β_2M) clearance by low-flux and high-flux dialysers reprocessed with various germicides.
LE	II-I
Number of patients & Patient characteristics	Total number of patients: 1,189. • Low flux arm (n=591 patients) • High flux arm (n=598 patients) Body weights, volumes of distribution of urea, blood flow rates, dialysate flow rates, treatment session durations, and ultrafiltration rates were all similar between the high-flux and low-flux groups. By design, mean ± SD β_2M clearance over all reuse sessions for patients in the high-flux group (34.6 ± 14.3 ml/min) was approximately 11-fold higher than that in the low-flux group (3.1± 8.1 ml/min).
Intervention	Reuse dialyser • High flux dialyser : (CT190 ;cellulose triacetate membrane, and F80 series; polysulfone membrane) • Low flux dialyzer:(CA series; cellulose acetate membrane, and F8 polysulfone membrane) ✓ Germicides used: ✓ Peroxyacetic acid/acetic acid/hydrogen peroxide combination (Renalin®) ✓ Bleach in conjunction with formaldehyde, gluteraldehyde or Renalin ✓ Heated citric acid ✓ Frequency of reuse of dialyser: ✓ Maximum number of times originally set at 20 ✓ For dialysis units using Renalin without bleach, 6 to 10
Comparison	-
Length of follow up	

Outcome measures/ Effect size	**β_2M Clearance by High-Flux and Low-Flux Dialysers during first use** Low-flux model (mean ± SD), β_2M clearance were below 10 ml/min: ✓ CA210 (3.1 ± 11.0 ml/min) ✓ F8 (1.7 ± 11.3 ml/min) High-flux model (mean ± SD), β_2M clearance were more variable: ✓ F80B (14.2 ± 13.4 ml/min) ✓ CT190 (42.3 ± 12.5 ml/min) **Effect of Renalin without Bleach on β_2M Clearance** • High-flux model, CT190 dialysers (mean ± SEM): ✓ Decreased in β_2M clearance between 1st use and the 10th through 14th reuses (67.2 % ± 2.7%) ✓ Did not decrease further when reuse was extended to 15 to 20 times • High-flux model, F80A dialysers: ✓ Decreased in β_2M clearance (- 0.64 ± 0.26 ml/min per reuse; P = 0.013 before June 15, 1997 and - 0.31 ± 0.31 ml/min per reuse; P = 0.32 after June 15, 1997) **Effect of Bleach on β_2M Clearance** • High-flux model, F80B dialysers (Mean ± SEM): ✓ Rate of increase of β_2M clearance with reused differed significantly (P < 0.001) among the three germicides • High-flux model ,CT190 dialysers (Mean ± SEM): ✓ When bleach was used in conjunction with either formaldehyde or Diacide, modest increased in β_2M clearance were observed (0.29 ± 0.11 ml/min per reuse; P = 0.011) • Low-flux dialysers: ✓ When reprocessed using any procedure that included bleach, there was a small but statistically significant increase in β_2M clearance during reuse (0.25 ± 0.07 ml/min per reuse; P < 0.001) ✓ Rate of increase in β_2M clearance did not differ significantly among formaldehyde, Diacide, and Renalin **Effect of Reuse on Urea Clearance** • High-flux dialysers (mean ± SEM): ✓ Decreased (-1.9 ± 0.3%) per 10 reuses (P < 0.001) with no significant differences among various types of dialysers and reprocessing methods (P = 0.096) • Low-flux dialysers(mean ± SEM): ✓ Decreased (-1.00 ± 0.3% per 10 reuses (P < 0.001) but the decrease was slightly lower than that of high-flux dialysers (P = 0.015) for all low-flux dialysers combined versus all high-flux dialysers combined). ✓ No significant differences in decreases of urea clearances between Renalin (-1.1 ± 0.4% per 10 reuses) and bleach containing methods (-1.2 ± 0.4% per 10 reuses) **Authors conclusion** Clearance of β_2M decreased, remain unchanged, or increased substantially with reuse, depending on both the membrane material and the reprocessing technique. In contrast, urea clearance decreased slightly (approximately 1% to 2% per 10 reuses), albeit statistically significantly with reuse, regardless of the porosity of the membrane and reprocessing method.
General Comments	Quality assessment (CASP) 1. Yes 2. Yes 3. Can't tell 4. Can't tell 5. Yes 6. Yes 7. Mean± SD, Mean ± SEM

Evidence Table : Membrane integrity
Question : Does reuse of dialyser affect dialyser performance?

Bibliographic citation	2. Leypoldt JK, Cheung AK, Deeter RB. Effect of hemodialyzer reuse: dissociation between clearances of small and large solutes. American Journal of Kidney Diseases. 1998;32(2):295-301
Study type / Methods	Cross over study of haemodialysis patients from the University of Utah Dialysis Program. The objective of the study was to evaluate the effect of extensive reprocessing using Renalin on small and large solute clearances measured directly across the dialyser for two types of commonly used low-flux and two types of commonly used high-flux dialysers. Haemodialysis was performed on each patient using four different dialysers on separate occasions. Each dialyzer was used exactly 15 times over a 5-week period before switching to another type of dialyser. The dialyser s were assigned to each patient in random order. Solute clearances were determined for each dialyser on use number 1,2,5 and 15.
LE	II-3
Number of patients & Patient characteristics	Total number of patients: 6 patients. • 3 men • 3 women • Mean age was 58 years (range, 25 to 79 years)
Intervention	Reuse dialyser • Low flux dialyser: (TAF175 containing cuprammonium membrane and CA210 containing cellulose acetate membrane) • High flux dialyser : (CT190G containing cellulose triacetate membrane and F80A containing polysulfone membrane) • Dialyser reprocessing was performed by an automated machine Renatron using Renalin at a concentration of 3% as the germicide
Comparison	-
Length of follow up	
Outcome measures/ Effect size	**Effect of Reuse on Urea, Creatinine and Phosphate Clearance (small solute)** • High-flux dialysers and low flux dialysers during use numbers; 1, 2, 5 and 15: ✓ Urea, creatinine, phosphate clearances were generally slightly greater for high-flux than for low-flux dialysers ✓ Decreasing trend in Urea, creatinine, phosphate clearances with reprocessing, but not significant **Effect of Reuse on β_2M and dialysate total protein concentration clearance (large solute)** • Low-flux dialysers during use numbers; 1, 2, 5 and 15: ✓ β_2M clearance and dialysate total protein concentration was small ✓ No significant difference were detected with reprocessing • High-flux dialysers during use numbers; 1, 2, 5 and 15: ✓ β_2M clearance and dialysate total protein concentration decreased with dialyser reprocessing (reuse versus first use, $P < 0.05$) **Authors conclusion** The observation showed that the maintenance of small solute clearances during reuse of high-flux dialysers does not ensure the maintenance of large solute clearance. Dialyser total cell volume of reprocessed high-flux dialysers cannot be used to predict clearances of large solutes.
General comments	

Evidence Table : Membrane integrity
Question : Does reuse of dialyser affect dialyser performance?

Bibliographic citation	3. Kerr PG, Argiles A, Canaud B, Flavier JL, Mion C. The effects of reprocessing high-flux polysulfone dialyzers with peroxyacetic acid on β_2 Microglobulin removal in hemodiafiltration. American Journal of Kidney Diseases.1992; XIX(5):433-438
Study type / Methods	Cross-sectional study in France. The objective of the study was to assess whether prolonged use (up to 20 uses) of polysulfone dialysers after peroxyacetic acid reprocessing reduced the amount of β_2M removed in a dialysis session. The patient records of all patients in haemodiafiltration (HDF) unit were analysed. The results of all patients commencing HDF before mid-1989 were included and subsequently the years 1989 and 1990 were analysed. The results were grouped in 3-month blocks, with 24 patients being included and 174 3-month blocks analysed.
LE	II-3
Number of patients & Patient characteristics	Total number of patients: 24 patients. ● Mean age was 60.2 ± 2.9 years (range, 32 to 81) ● Period of dialysis =77 ± 15 months
Intervention	Reuse dialyser ● High flux polysulfone dialyser ● Dialyser reprocessing was performed using Renatron machine supplied with peroxyacetic acid as the cleansing and sterilising agent. ● Dialysers were discarded if they failed either the pressure or volume test or after a maximum of 20 uses was achieved. ● The first, second, 10th and 20th sessions were analysed.
Comparison	
Length of follow up	

Outcome measures/ Effect size	**Effect of Reuse on Urea, Creatinine, β_2M and retinol-binding protein (RBP)**
	
	Percent reduction of serum urea and creatinine up to 20 uses of high flux polysulphone dialysers (Mean ± SEM):
	✓ No significant difference in the percent reduction of these molecules for up to 20 uses:-
	  ✓ Urea [1st use (68.9 ± 1.1%) and 20th use (66.3 ± 2.4%)]
	  ✓ Creatinine [1st use (63.9 ± 1.3) and 20th use (64.9 ± 2.7%)]
	
	Percent reduction of β_2M and RBP up to 20 uses of high flux polysulphone dialysers (Mean ± SEM):
	✓ β_2M (significant decrease in the percent reduction when use no. 10 or no. 20 compared with use no.1 or no. 2):-
	  ✓ 1st use (71.8 ± 1.1%), 10th use (66.8 ± 1.5%), and 20th use (66.8 ± 2.2%), $P < 0.05$]
	✓ RBP (significant decrease in the percent reduction when use no. 20 compared with use no.1):-
	  ✓ 1st use (18.6 ± 2.1%) and 20th use (11.2 ± 2.4%), $P < 0.05$]
	
	Authors conclusion
	Reprocessing of polysulfone dialysers for HDF with peroxyacetic acid up to 20 times does not interfere with the ability to remove urea, creatinine, and proteins beyond a molecular weight of 12,000 (including β_2M in the course of dialysis**.**

General comments	

Evidence Table : Membrane integrity
Question : Does reuse of dialyser affect dialyser performance?

Bibliographic citation	4. Quseph R, Smith BP, Ward RA. Maintaining blood compartment volume in dialysers reprocessed with peracetic acid maintains Kt/V but not β_2 Microglobulin removal. American Journal of Kidney Diseases.1997;30 (4):501-506
Study type / Methods	Cross-sectional study in the U.S. The objective of the study was to test the hypothesis that clearance of small and large solutes remain at 90% or greater of their initial values provided the blood compartment volume remain at 80% or greater of its initial value for dialysers containing cellulose and synthetic membranes processed for reuse with a peracetic acid/hydrogen peroxide mixture.
LE	II-3
Number of patients & Patient characteristics	2 studies: • 1st study:- ✓ 8 men ✓ Average age, (53 ± 12 years) ✓ Average duration of dialysis (59 ± 33 months) • 2nd study:- ✓ 9 (3 men and 6 women) ✓ Average age, (59 ± 9 years) ✓ Average duration of dialysis (40 ± 25 months)
Intervention	Reuse dialyser • AM-UP-75WET dialyser which contain 1.5 m^2 of regenerated cellulose membrane (high -flux)- 1st study • F80B dialyser which contain 1.8 m^2 of polysulfone membrane (high- flux) • In both studies, dialysers were reprocessed for reuse using an automated system (Renatron) and Renalin as the cleaning and disinfecting agent and sterilising agent. • Dialysers were rejected for subsequent use if the blood compartment volume was 80% or less of the initial value.
Comparison	
Length of follow up	
Outcome measures/ Effect size	**Effect of Reuse With Peracetic Acid /Hydrogen Peroxide on urea removal (Kt/V), Blood Compartment Volume and β_2M for AM-UP-75WET (regenerated cellulose membrane) dialyser:-** ✓ Blood compartment volumes remained greater than 80% of the initial value after 12 treatments for all 8 patients (Mean ± SD):- ✓ [1st use (98.5 ± 2.0%) and 12th use (90.2 ± 6.8%)] ✓ Urea removal (Kt/V) did not change with reuse, Single-pool:- [1st use (1.25 ± 0.09) and 12th use (1.19 ± 0.11)] ✓ Reduction of β_2M concentration decreased with reuse but not significant (Mean ± SD):- ✓ [1st use (18 ± 9%), 4th use (19 ± 6%), 12th use (12 ± 11%), P = 0.276] **Effect of Reuse With Peracetic Acid /Hydrogen Peroxide on urea removal (Kt/V), Blood Compartment Volume and β_2M for F80B (polysulfone membrane) dialyser:-** ✓ Blood compartment volumes remained greater than 80% of the initial value after 10 treatments for all 9 patients. However, the volume of 4 of these dialysers subsequently decreased to 80% of the initial value so only 5 dialysers completed 15 treatments ✓ Urea removal (Kt/V) did not change with reuse, Single-pool:- [1st use (1.58 ± 0.21) and 15th use (1.50 ± 0.17)] ✓ Reduction of β_2M concentration decreased significantly as the number of uses increased (P = 0.042) ✓ The reduction of β_2M concentration decreased from 30 ± 12% during 1st use to 12 ± 10% during the tenth use (P < 0.05) **Authors conclusion** The removal of urea is maintained during reuse with peracetic acid/hydrogen peroxide provided the blood compartment volume remains 80% of its initial value. However, removal of β_2M may not be maintained, even though blood concentration compartment volumes remain at 80% of their initial value.
General comments	

Evidence Table : Membrane integrity
Question : Does reuse of dialyser affect dialyser performance?

Bibliographic citation	5. Fleming SJ, Foreman K, Shanley K, Mihrshahi R, Siskind V. Dialyser reprocessing with Renalin®. Am J Nephrol.1991;11:27-31
Study type / Methods	Cross-sectional study in 11-bed chronic dialysis centre in Royal Brisbane Hospital, Australia. The objective of the study was to examine the effect of reprocessing dialysers with Renalin on patient well-being and dialyser performance. 2,759 dialysis in 59 patients were studied in 6 month period.
LE	II-3
Number of patients & Patient characteristics	• 59 adult, stable, chronic patients 937 female, 22 male) with a median age of 65 years (range 24 to 78) undergoing in-hospital haemodialysis. • 2,759 dialysis
Intervention	Reuse dialyser ✓ Four hollow-fibre dialysers: • TAF 08 (Terumo Corp.) • TAF 12 (Terumo Corp.) • CA-90 (Baxter Healthcare) • C_DAK 4000 (CD Medical) ✓ Automated dialyser reprocessing was performed with Renatron and the sterilant used was Renalin.
Comparison	
Length of follow up	
Outcome measures/ Effect size	• **Number of reuses of dialysers:** ✓ Mean number of uses was 4.5 ✓ Most dialysers were withdrawn after 6 uses ✓ Dialyser survival varied with the type of dialyser but unaffected by the dialysate base • **Mean in vivo clearances of urea, creatinine and phosphate:** ✓ No significant difference (P > 0.05);- - [Urea; 1st use (158.1 ml/min), 6th use (156.5 ml/min) - [Creatinine; 1st use (137.1 ml/min), 6th use (134.6 ml/min) - [Phosphate; 1st use (120.4 ml/min), 6th use (116.3 ml/min) • **Dialyser ultrafiltration characteristics:** ✓ Significant decrease from mean of 3.3 ml/h/mmHg on first use to 3.1 ml/h/mm Hg on the sixth use (P < 0.05) • **Mean number of symptoms per treatment per patients:** ✓ New dialyser versus reprocessed dialysers (0.63 versus 0.50, P < 0.001)
General comments	

Evidence Table : Membrane integrity
Question : Does reuse of dialyser affect dialyser performance?

Bibliographic citation	6. Sherman RA, Cody RP, Rogers ME, ME, Solanchick JC. American Journal of Kidney Diseases. 1994;24(6):924-926
Study type / Methods	Cross-sectional study in ESRD Network (New Jersey, Puerto Rico, and the Virgin Islands). Objective of the study was to assess the effect of dialyser reuse in an uncontrolled clinical practice setting. All patients underwent formal urea kinetic modelling monthly, usually for 3 sequential months. Dialyser was reprocessed and reused in the usual manner for each of prior uses. For each patient, Kt/V urea for the treatment using the dialyser with the most reuses (mean; 13.8) was compared with the treatment using the dialyser with the fewest reuses (mean;3.8).
LE	II-3
Number of patients & Patient characteristics	436 haemodialysis patients in 34 study centres
Intervention	Reuse dialyser ✓ Dialyser reprocessed using: • Formalin in 23 centres (325 patiens) • Renalin in 5 centres (48 patients) • Gluteraldehyde in 6 centres (63 patients) ✓ Automated or manual dialyser reprocessing
Comparison	
Length of follow up	3 months
Outcome measures/ Effect size	✓ **Number of reuses of dialysers:** ✓ Reuse treatments were performed with dialysers that has been processed an average of 9.8 times ✓ Number of dialysers uses for the "high reuse" treatments was 13.8 ✓ Number of dialysers uses for the "low reuse' treatments was 3.8 ✓ **Mean Kt/V for high reuse treatments (13.8) versus low reuse treatments (3.8):** ✓ The mean Kt/V delivered for high reuse treatments were significantly lower than that for low reuse treatments [(1.05 versus 1.10, P = 0.002)] ✓ Prescribed Kt/V in high and low reuse treatments was identical (1.21 for both groups) ✓ With formalin reuse, the mean delivered Kt/V for high reuse versus low reuse was (1.02 versus 1.08, P = 0.002) ✓ With Renalin reuse, the mean delivered Kt/V for high reuse versus low reuse was (1.08 versus 1.16, P = not significant) ✓ With Gluteraldehyde (1.21 versus 1.19, P = not significant) **Authors conclusion** Dialyser reprocessing significantly impairs dialysis delivery, an effect that may be related to the methods and procedures in individual dialysis centres.
General comments	

Evidence Table : Membrane integrity
Question : Does reuse of dialyser affect dialyser performance?

Bibliographic citation	7. Matos JPS, Andre MB, Rembold SM, Caldeira FER, Lugon JR. Effects of dialyser reuse on the permeability of low-flux membranes. American Journal of Kidney Diseases. 2000;35(5):839-844
Study type / Methods	Prospective, non randomised cross over design in Brazil. The objective of the study was to evaluate the effect of reuse on the permeability of low-flux membrane to solutes of different molecular weights. Each patient was treated with low-flux polysulfone (synthetic) and cellulose diacetate (unmodified cellulose) membrane dialysers reprocessed with either 4% formaldehyde or peracetic acid and hydrogen peroxide. Dialysers were assessed at reuses 0 (1st use), 6 (7th use), and 12 (13th use).
LE	II-3
Number of patients & Patient characteristics	5 patients undergoing in-centre daily haemodialysis.
Intervention	Reuse dialyser (low- flux) ● Combination of membrane and sterilant: ✓ Polysulphone membrane reprocessed with formaldehyde ✓ Polysulphone membrane reprocessed with peracetic acid ✓ Cellulose diacetate membrane reprocessed with formaldehyde ✓ Cellulose diacetate membrane reprocessed with peracetic acid
Comparison	
Length of follow up	
Outcome measures/ Effect size	**Effect of Dialyser Reuse on the permeability of low-flux (cellulose diacetate and polysulfone) membranes** ✓ **Total cell volume:** ✓ After 12 reuses, reduced in both cellulose diacetate and polysulphone dialysers irrespective of the sterilant used, but significant difference only for cellulose diacetate ($P < 0.05$ versus reuse 0) ✓ **Hydraulic ultrafiltration coefficient (K_{UF}):** ✓ Cellulose diacetate dialysers reprocessed with either formaldehyde or peracetic acid showed reduction in K_{UF} [31%, ($P < 0.05$) and 23% ($P < 0.05\%$) respectively] ✓ A significant elevation in K_{UF} was found in polysulfone membranes reprocessed with peracetic acid (41%; $P < 0.05$), but no alteration in K_{UF} were found in polysulfone membranes reprocessed with formaldehyde ✓ **Sieving coefficient for β_2M:** ✓ Cellulose diacetate membranes were intrinsically more permeable to β_2M than polysulfone membranes (sieving coefficient, 6.85 ± 2.53 versus $0.04 \pm 0.02 \times 10^{-2}$; $P < 0.001$), which is not modified by any of the sterilants
General comments	

Evidence Table : Effectiveness
Question : Is Single use dialyser effective compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis ?

Bibliographic citation	1. Galvao TF, Silva MT, Araujo ME, Bulbol WS, Cardaso AL. Dialyzer reuse and mortality risk in patients with end-stage renal disease: A systematic review. Am J Nephrol.2012;35(3):249-258. Doi:10.1159/000336532.
Study type / Methods	Systematic Review The objective of this review was to evaluate the effect of dialyser reuse on the mortality of patients with end-stage renal disease compared to patients with single-use dialysers. MEDLINE, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Latin American and Carribean Centre on Health Sciences Information (LILACS), Scientific Electronic Library Online (SciELO), United States Renal Data System 2011 Annual Data Report (USRDS ADR), universities theses, and the annals of congress of major nephrology societies were searched. Grey literature was also searched. References of relevant articles were screened. Last literature search was conducted in January 2012. Four pairs of researches independently selected trials for inclusion. Data from each included trial were extracted by one of the three researchers and the other two confirmed the extraction. The quality of the included studies was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.
LE	
Number of patients & Patient characteristics	**A total of 14 studies were included in the review** (Held 1987, Held 1994, Feldman 1996, Collins 1998, Feldman 1999, Ebben 2000, Port 2001, Collins 2004, Lowrie 2004, Fan 2005, Chuang 2008, Lacson 2011, Bond 2011, USRDS 2011:- • 9 retrospective cohort • 4 prospective cohort • 1 single crossover • 13 studies conducted in USA • 1 study conducted in Taiwan • 8 studies conducted in 1980s to1990s • 5 studies conducted after 2000 **Health unit type:-** • 8 studies involved hospital and free standing • 5 studies involved freestanding • 1 study involved hospital **Dialyser Type:-** • 4 studies conventional • 5 studies conventional and synthetic • 3 studies synthetic • 2 studies- not reported **Membrane permeability:-** • 4 studies used low flux • 3 studies used low and high flux • 2 studies used high flux • 5 studies – not reported **Number of patients included:-** • 14 studies (total-956,807 patients) • Only one study (Chuang, 2008) had sample size < 1000 • The largest sample size is from the USRDS 2011 (245,538 patients treated in 2009, 110,299 reuse and 135,239 single use) **Funding:-** • 8 health department / agency for research (Held 1987,1994, Feldman 1996, 1999, Port 2001, Chuang 2008, Bond 2011, USRDS 2011) • 4 disinfectant manufacturer (Collin 1998, Ebben 2000, Collin 2004, Fan 2005) • 2 dialyser manufacturer (Lowrie 2004, Lacson 2011) The evidence was classified as very low quality (rated down from low (observational design) to very low.
Intervention	Reuse dialyser Disinfectant used:- • hypochlorite • formaldehyde • glutaraldehyde peracetic acid
Comparison	Single use dialyser
Length of follow up	

Outcome measures/ Effect size	**Mortality:-** **a. Relative Risk (RR), Hazard Ratio (HR), Odds Ratio (OR), Standardized Mortality Ratio (SMR) of reuse versus single use dialyser** • **Held, 1987 (All, 4,661 patients), hospital and freestanding:-** ✓ RR = 0.88, P < 0.03 (multiple uses started prior 1980) ✓ RR = 1.01, P < 0.88 (multiple - uses started after 1980) • **Held, 1994 (All, 66,097 patients), freestanding:-** ✓ [RR (95% CI) = 1.06 (0.99 to 1.14)] – used formaldehyde ✓ [RR (95% CI) = 1.17 (1.04 to 1.31)] – used gluteraldehyde ✓ [RR (95% CI)= 1.13 (1.06 to 1.21)] - used peracetic acid • **Feldman, 1996 (All, 27,939 patients):-** ✓ [RR (95% CI) = 1.06 (0.98 to 1.15)] – used formaldehyde, hospital ✓ [RR (95% CI) = 1.03 (0.96 to 1.10)] – used formaldehyde, freestanding ✓ [RR (95% CI) = 1.09 (0.71 to 1.67) – used gluteraldehyde, hospital ✓ [RR (95% CI) = 1.13 (0.95 to 1.35) – used gluteraldehyde, freestanding ✓ [RR (95% CI) = 0.95 (0.85 to 1.06)] – used peracetic acid, hospital ✓ [RR (95% CI) = 1.10 (1.02 to 1.18)] – used peracetic acid, freestanding • **Collin, 1998 (All, 13,551 patients):-** ✓ [RR (95% CI) = 1.15 (0.86 to 1.15)] – used formaldehyde, hospital ✓ [RR (95% CI) = 0.82 (0.72 to 0.93)] – used formaldehyde, freestanding ✓ [RR (95% CI) = 1.09 (0.74 to 1.59) – used gluteraldehyde, hospital ✓ [RR (95% CI) = 1.03 (0.80 to 1.33) – used gluteraldehyde, freestanding ✓ [RR (95% CI) = 0.94 (0.67 to 1.32)] – used peracetic acid, hospital ✓ [RR (95% CI) = 0.83 (0.72 to 0.96)] – used peracetic acid, freestanding • **Feldman, 1999 (All, 1,491 patients), freestanding:-** ✓ Adjusted for comorbidities [RR (95% CI) = 1.25 (1.03 to 1.52)] – used formaldehyde, gluteraldehyde and peracetic acid • **Ebben, 2000 (All, 374,744 patients) freestanding:-** ✓ No significant difference in mortality rates • **Port, 2001 (All, 12,791 patients), hospital and freestanding:-** ✓ Adjusted for DCF [RR (95% CI) = 0.96 (0.86 to 1.08)]

RR for mortality by reuse practice

- ✓ Peracetic acid mixture versus formalin:
  - [RR (95% CI) = 1.15 (0.99 to 1.30)]
- ✓ Low flux synthetic versus high flux synthetic membrane:
  - [RR (95% CI) = 1.24 (1.02 to 1.52)]
- ✓ Without than with bleach during reprocessing:
  - [RR 1.24 (95% CI) = (1.01 to 1.48)]

- **Collins, 2004 (All, 49,273 patients), hospital and freestanding:-**
  - ✓ [RR (95% CI) = 1.01 (0.92 to 1.11)] (used formaldehyde)
  - ✓ When used gluteraldehyde, peracetic acid and hypochlorite:
    – no significant difference
- **Fan, 2005 (All, 75,831 patients), hospital and freestanding:-**
  - ✓ Adjusted [HR (95% CI) = 0.98 (0.94 to 1.02)]
- **USRDS, 2011 (All, 245,538 patients), hospital and freestanding:-**
  - ✓ [SMR (95% CI) = 1.01 (0.99 to 1.02)]- Fresenius
  - ✓ [SMR (95% CI) = 0.97 (0.96 to 0.99)]- DaVita
  - ✓ [SMR (95% CI) = 0.96 (0.91 to 1.01)]- DCI
- **Bond, 2005 (All, 27,405 patients), freestanding:-**
  - ✓ Adjusted [HR (95% CI) = 1.04 (0.97 to 1.12)] -(used peracetic acid)

b. Hazard Ratio (HR), Odds Ratio (OR), of single use versus reuse dialyser

- **Lowrie, 2004 (All, 71,122 patients), freestanding:-**
  Case-mix plus lab Hazard ratio
  - ✓ [HR (95% CI) = 0.95 (0.90 to 1.01)]
    – Day 0
  - ✓ [HR (95% CI) = 0.95 (0.88 to 1.01)]
    – after 30 days
  - ✓ [HR (95% CI) = 0.92 (0.86 to 0.98)
    – after 60 days
  - ✓ [HR (95% CI) = 0.90 (0.84 to 0.99)
    – after 90 days
  - ✓ [HR (95% CI) = 0.90 (0.84 to 0.97)
    - after 120 days
    (used formaldehyde with hypochlorite, gluteraldehyde, peracetic acid, citric acid, heat)
- **Chuang, 2008 (All, 822 patients), hospital:-**
  - ✓ [OR (95% CI) = 2.94 (1.56 to 5.55)]
    (used peracetic acid)
    - Note: different inclusion criteria were applied for patients in the reuse and single use groups, resulting in statistically significant healthier patient profile in the reuse group
- **Lacson, 2011 (All, 2,613 patients), freestanding:-**

  Case-mix adjusted
  - ✓ [HR (95% CI) = 0.74 (0.56 to 0.89)]
    (used peracetic acid)

Authors conclusion
No significant differences were identified for the superiority or inferiority of dialyser reuse versus single use when assessing the mortality of patients with end-stage renal disease. Studies of higher quality, including randomised clinical trials are required to provide conclusive evidence regarding the effectiveness and safety of dialyzer reuse.

General comments

Evidence Table : Effectiveness
Question : Is Single use dialyser effective compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis ?

Bibliographic citation	2. Feldman HI, Bilker WB, Hackett MH, Simmons CW, Holmes JH, Pauly MV, Escarce JJ. Association of dialyzer reuse with hospitalization rates among hemodialysis patients in the US. Am J Nephrol.1999;19(6):641-648
Study type / Methods	Cohort study The objective of the study was to determine If reuse of haemodialysers is associated with higher rates of hospitalisation and their resulting costs among end-stage renal disease (ESRD) patients. Study of hospitalisation rates among 27,264 ESRD patients beginning haemodialysis in the United States in 1986 and 1987 in free-standing and hospital- based dialysis facilities Principal outcome:- Hospitalisation from any cause. Secondary outcomes were:- i. Hospitalisation for causes other than morbidity associated with dialysis vascular access ii. Hospitalisation for any blood-borne infection Rate ratios of hospitalisation were calculated using Poisson regression and reported with 95% confidence interval (CI). A complementary secondary analysis using Cox proportional hazards regression was also performed to examine the robustness of the principal analysis. Poison regression models were constructed separately for patients in hospital-based units and for patients in free-standing units for the 3 hospitalisation outcomes. • Model A: compared reuse to single-use dialysis, model • Model B: compared individual sterilants to single-use dialysis • Model C: compared sterilants to one another
LE	II-2
Number of patients & Patient characteristics	Total 27,264 patients:- • 18,679 treated in free-standing dialysis facilities (68.5%) • 8,585 treated in hospital-based facilities (31.5%) • 86.5% of patients in free-standing dialysis facilities reuse dialyser • 43.3% % of patients in Hospital-based dialysis facilities reuse dialyser • Overall, 52.2% were males • Above 18 years of age • Mean (SD) age among subjects in free-standing facilities = 61.1 (15.4) • Mean (SD) age among subjects in hospital-based facilities = 61.2 (15.7) Causes of ESRD:- • Diabetes mellitus (32.3%) • Hypertension (31.6%) • Glomerulonephritis (13.6%)

Intervention	Reuse dialyser Sterilant for reuse in free-standing facilities:- • Peracetic acid and acetic acid (PAA) - 26.2% • Formaldehyde – 69.5% • Gluteraldehyde - 3.4% • Missing – 0.9% Sterilant for reuse in hospital-based facilities:- • Peracetic acid and acetic acid - 34.3% • Formaldehyde - 62.6% • Gluteraldehyde - < 0.1% • Missing < 0.1%
Comparison	Single use dialyser
Length of follow up	Followed-up from onset of ERSD until death, transplantation, a switch to treatment with outpatient peritoneal dialysis, or June 30, 1991, whichever occurred first.
Outcome measures/ Effect size	**1. Hospitalisation for any cause** **a. Free-standing dialysis unit** • **Model A:** ✓ Reuse versus single use - [RR (95% CI) = 1.08 (1.02 to 1.14), P = 0.01] • Adjusted mean hospitalisation rates for patients exposed to reuse dialysis and for patients expose to single use were 2.25/ year and 2.19/year respectively. • **Model B:-** ✓ Formaldehyde versus single use - [RR (95% CI) = 1.07 (1.00 to 1.14), P = 0.04] ✓ PAA versus single use - [RR (95% CI) = 1.11 (1.04 to 1.18), P < 0.01] ✓ Gluteraldehyde versus single use - [RR (95% CI) = 1.00 (0.89 to 1.13), P = 0.97] • Adjusted mean rates of hospitalisation were 2.32/year for combination of peracetic acid and acetic acids, 2.23/year for formaldehyde, 2.09/year for gluteraldehyde. • **Model C:-** ✓ PAA versus formaldehyde - [RR (95% CI) = 1.04 (0.99 to 1.10), P = 0.14] ✓ PAA versus Gluteraldehyde - [RR (95% CI) = 1.11 (0.99 to 1.25), P = 0.09] **b. Hospital-based dialysis unit** • **Model A:** ✓ Reuse versus single use - [RR (95% CI) = 1.00 (0.94 to 1.08), P = 0.90] • **Model B:-** ✓ Formaldehyde versus single use - [RR (95% CI) = 1.01 (0.92 to 1.09), P = 0.90] ✓ PAA versus single use - [RR (95% CI) = 1.00 (0.90 to 1.12), P = 0.96] ✓ Gluteraldehyde versus single use - [RR (95% CI) = 0.99 (0.78 to 1.25), P = 0.91] • **Model C:-** ✓ PAA versus formaldehyde - [RR (95% CI) = 1.00 (0.88 to 1.13), P = 0.98] ✓ PAA versus Gluteraldehyde - [RR (95% CI) = 1.02 (0.79 to 1.32), P = 0.89]

	2. Hospitalisation for causes other than morbidity associated with dialysis vascular access **a. Free-standing dialysis unit** • **Model A:** ✓ Reuse versus single use - [RR (95% CI) = 1.06 (1.00 to 1.13), P = 0.04] • **Model B:-** ✓ Formaldehyde versus single use - [RR (95% CI) = 1.04 (0.98 to 1.11), P = 0.19] ✓ PAA versus single use - [RR (95% CI) = 1.13 (1.05 to 1.20), P < 0.01] ✓ Gluteraldehyde versus single use - [RR (95% CI) = 1.01 (0.90 to 1.15), P = 0.83] • **Model C:-** ✓ PAA versus formaldehyde - [[RR (95% CI) = 1.08 (1.03 to 1.15), P< 0.01] ✓ PAA versus Gluteraldehyde - [[RR (95% CI) = 1.11 (0.98 to 1.25), P = 0.10] **b. Hospital-based dialysis unit** • **Model A:** ✓ Reuse versus single use - [RR (95% CI) = 1.00 (0.94 to 1.08), P = 0.90] - [RR (95% CI) = 0.99 (0.78 to 1.25), P = 0.91] • **Model B:-** ✓ Formaldehyde versus single use - [RR (95% CI) = 1.02 (0.94 to 1.11), P = 0.60] ✓ PAA versus single use - [RR (95% CI) = 1.01 (0.90 to 1.14), P = 0.87 ✓ Gluteraldehyde versus single use - [RR (95% CI) = 0.97 (0.77 to 1.22), P = 0.79] • **Model C:-** ✓ PAA versus formaldehyde - [RR (95% CI) = 1.00 (0.88 to 1.13), P = 0.98] ✓ PAA versus Gluteraldehyde - [RR (95% CI) = 1.05 (0.81 to 1.38), P = 0.70] **3. Hospitalisation for blood-borne infection** • Analysis of hospitalisation for blood-borne infection failed to detect any significant relationships between dialyser reuse or specific sterilants and the rate of hospitalisation in either free-standing or hospital-based facilities. **Authors conclusion:** Dialysis in free-standing facilities reprocessing dialysers with peracetic acid / acetic acids or formaldehyde was associated with greater hospitalisation than dialysis without dialyser reprocessing. This greater hospitalisation accounts for large increment of inpatient stays in the USA. These findings raise important concerns about potentially avoidable morbidity among haemodialysis patients.
General comments	Quality assessment (CASP) 1. Yes 2. Yes 3. Yes 4. Yes 5. Can't tell (not mentioned about blinding) 6. Yes 7. Yes 8. RR, 95% CI 9. CI is not wide

Evidence Table : Effectiveness
Question : Is Single use dialyser effective compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis ?

Bibliographic citation	3. Feldman HI, Bilker WB, Hackett MH, Simmons CW, Holmes JH, Pauly MV, Escarce JJ. Association of dialyzer reuse with hospitalization and survival rates among U.S. hemodialysis patients: Do Comorbidities Matter? J Clin Epidemiol.1999;52(3):209-217
Study type / Methods	Cohort study The objective of the study was to determine whether the associations between reuse of haemodialysers and higher rates of death and hospitalisation persist after adjustment of comorbidity. Study of survival and hospitalisation rates among 1,491 U.S chronic haemodialysis patients beginning treatment in 1986 and 1987 in free-standing dialysis facilities. Rate ratios of hospitalisation were calculated using Poisson regression and reported with 95% confidence interval (CI) The impact of dialyzer reuse was compared across three survival models: i. An unadjusted model ii. A "base" model adjusted for age, race, gender and renal diagnosis iii. An "augmented" model adjusted for age, race, gender, renal diagnosis and baseline comorbidity which included history of myocardial infarction, coronary artery revascularisation, congestive heart failure, arrhythmias, and any cancer, as well as serum creatinine and serum albumin.
LE	II-2
Number of patients & Patient characteristics	Total 1,491 subjects:- • 1,241reuse subjects (83.2%) • 250 single use subjects (16.8%) • 51.3% males • 48.7% females Causes of ESRD:- • Diabetes mellitus (30.5%) • Hypertension (33.6%) • Glomerulonephritis (13.4%) • Other diagnosis (22.5%)
Intervention	Reuse dialyser Sterilant for reuse:- • Peracetic acid and acetic acid (PAA) - 27.8% • Formaldehyde (52.9%) • Gluteraldehyde (3.0%)
Comparison	Single use dialyser
Length of follow up	Followed-up from onset of ERSD until death, transplantation, a switch to treatment with outpatient peritoneal dialysis, or June 30, 1991, whichever occurred first.

Outcome measures/ Effect size	**Hospitalisation for any cause** **a. Reuse versus single use** • **Unadjusted model** ✓ [RR (95% CI) = 1.40 (1.17 to 1.67), P < 0.001] • **Base model** ✓ [RR (95% CI) = 1.35 (1.17 to 1.56), P < 0.001] • **Augmented model** ✓ [RR (95% CI) = 1.37 (1.17 to 1.58), P < 0.001] **b. Formaldehyde versus single use** • **Unadjusted model** ✓ [RR (95% CI) = 1.25 (1.06 to 1.47), P = 0.009] • **Base model** ✓ [RR (95% CI) = 1.21 (1.05 to 1.41), P = 0.009] • **Augmented model** ✓ [RR (95% CI) = 1.25 (1.09 to 1.43), P = 0.002] **c. PAA versus single use** • **Unadjusted model** ✓ [RR (95% CI) = 1.42 (1.17 to 1.74), P < 0.001] • **Base model** ✓ [RR (95% CI) = 1.37 (1.13 to 1.66), P = 0.001] • **Augmented model** ✓ [RR (95% CI) = 1.40 (1.17 to 1.66), P < 0.001] **Authors conclusion:** Higher rates of death and hospitalisation associated with dialyser reuse persist regardless of adjustment for demographic characteristics or baseline comorbidities. These findings amplify concerns that there exists elevated morbidity among haemodialysis patients treated in facilities that reuse haemodialysers. Although the association we observed were not confounded by morbidity, a cause-and-effect relationship between dialyser reuse and morbidity could not be proved because of the inability to control for aspects of care other than dialyser reuse.
General comments	

Evidence Table : Effectiveness
Question : Is Single use dialyser effective compared to reuse dialyser for patients with End-Stage Renal Disease undergoing haemodialysis ?

Bibliographic citation	4. Held PJ, Wolfe RA, Gaylin DS, Port FK, Levin NW, Turenne MN. Analysis of the association of dialyzer reuse practices and patient outcomes. American Journal of Kidney Diseases.1994;23(5):692-708
Study type / Methods	Cohort study The objective of the study was to assess the relationship between dialyser reuse practices and haemodialysis patient mortality through one year of follow-up. Medicare patient demographic and survival data were combined with dialyzer reuse data from the Centres for Disease Control and Prevention's annual survey of dialysis-related diseases. Data were analysed for the US Medicare haemodialysis population of never transplanted patients prevalent on January 1, 1989, and January 1, 1990 who were treated in free-standing dialysis unit that used primarily conventional (not high flux) dialyzers. Time to mortality, or transplant, and other censoring on December 31st of each year was regressed with proportional hazards models on patient, dialysis unit, and reuse measures. Age, race, and diagnosis-standardized mortality ratios for dialysis units were also regressed with weighted least squares techniques against dialysis unit and reuse measures.
LE	II-2
Number of patients & Patient characteristics	Total 66,097 patients:- • 53,634 reuse (81.2%) • 12,463 non reuse (single use) - (18.8%) • 49% males • 51% females • Mean age =59.9 years Causes of ESRD:- • Diabetes mellitus (28%) • Hypertension (33%) • Glomerulonephritis (15%) • Other diagnosis (24%)
Intervention	Reuse dialyser Conventional low-flux dialysers Sterilant for reuse:- • Peracetic acid mixture (PAM) - 38.6% • Formalin (formaldehyde) - 55.9% • Gluteraldehyde -5.5%
Comparison	Single use dialyser
Length of follow up	1 year
Outcome measures/ Effect size	**Hospitalisation for patients treated in "low-flux" freestanding dialysis units.** • **PAM versus non reuse (single use)** ✓ [RR = 1.11, P < 0.01] • **Glutaraldehyde versus non reuse (single use)** ✓ [RR = 1.12, P < 0.03] • **Formalin versus non reuse (single use)** ✓ [RR = 1.04, P = 0.29]
General comments	Quality assessment (CASP) 1. Yes 2. Yes 3. Yes 4. Yes 5. Can't tell (not mentioned about blinding) 6. Can't tell. 7. Can't tell 8. RR, P value 8. CI is not mentioned

Evidence Table : Economic

Question : Is single use dialyser cost-effective compared to reuse dialyser for haemodialysis of patients with end-stage renal disease (ESRD)?

Bibliographic citation	1. Manns BJ, Richardson RMA, Donaldson C. To reuse or not to reuse? An economic evaluation of hemodialyzer reuse versus conventional single-use hemodialysis for chronic hemodialysis patients. International Journal of Technology Assessment in Health Care.2002;18(1):81-93
Study type / Methods	Economic evaluation (cost-utility analysis) conducted in Canada. The aim of this study was to evaluate the cost-effectiveness of reusing haemodialysers for patients with kidney failure on dialysis employing either a heated citric acid or formaldehyde sterilization method, in comparison to the standard practice of single-use dialysis. A simulated cohort of haemodialysis patients whose characteristics were representative of local patients seen in a Canadian dialysis centre in terms of age, sex and comorbidity were evaluated. For baseline analysis, they assumed that reuse would be performed for a dialysis unit containing 320 patients (i.e. the number of patients who receive haemodialysis at the Foothills Medical Centre in Calgary, Canada). The treatment alternatives considered in the analysis consists of all the treatment options that are currently used in Canada. A decision tree was constructed to model the effect of three different haemodialysis options on the costs and quality-adjusted life expectancy of 'typical' haemodialysis patients. A Markov process was used to model yearly transitions between the three possible clinical states: a) alive on haemodialysis; b) alive with renal transplant; and c) dead. **A 5-year time horizon** was considered in the base-case analysis since the minority of patients remain on haemodialysis at 5 years. The horizon was extended in sensitivity analysis. The model outputs were quality-adjusted life-years (QALYs) and costs. QALYs were estimated by multiplying the number of cycles spent by the average patients in each clinical state by the utility associated with the state. Costs and QALYs were both discounted at an annual rate of 5%. **Data sources** **Mortality:** The annual mortality of haemodialysis patients on synthetic dialysers was estimated using the mean annual mortality risk reported for all Canadian haemodialysis patients by the Canadian Organ Replacement Register (CORR). A meta-analysis of all relevant studies was performed to determine whether the haemodialyser reuse was associated with increased relative risk of mortality or hospitalisation. **Health-related Quality of Life** Information on the average utility score for patients treated with haemodialysis or renal transplantation was estimated from a study by using the time-trade off technique. **Costs** **The study took the perspective of healthcare payer**. The cost of heated citric acid was estimated from the centre experienced with the technique. The cost of end-stage renal disease (ESRD) care, survival data, and patient utilities were estimated from published sources. **Implications on costs and QALYs were considered for four potential scenarios (Scenarios 1,2,3 and 4).** **Sensitivity analysis** One-way and two-way sensitivity analyses were performed on all variables in their model.
LE	
Number of patients & Patient characteristics	Baseline characteristics of all cohorts:-. - Mean age = 60.0 years - Sex = 50% male - Comorbidity= 40% diabetic, 40% with ischaemic heart disease
Intervention	Single use dialyser with a typical synthetic dialyser

Comparison	Reuse dialyser: • Reuse with heated citric acid and a synthetic dialyser designed for reuse • Reuse with formaldehyde and a synthetic dialyser designed for reuse
Length of follow up	
Outcome measures/ Effect size	**Cost-utility analysis** **a. Risk of mortality and hospitalisation** • Annual mortality risk for haemodialysis patients treated with synthetic single use = 0.152 (range: 0.145 to 0.159) • Annual number of days of hospitalisation for haemodialysis patients treated with synthetic single use = 7.4 days (range: 4.2 to 10.7 days) • Average utility score: ✓ 0.43 (range; 0.35 to 0.51) for in-centre haemodialysis patients ✓ 0.84 (range; 0.79 to 0.89) for patients with renal transplant • Annual rate of transplantation = 0.0835 • Annual mortality risk for transplant patients = 0.045 • RR of mortality: ✓ 1.01 (range; 0.996 to 1.027) for any method of haemodialyser reuse versus synthetic single use ✓ 1.002 (range:0.99 to 1.016) for patients treated with formaldehyde reuse versus synthetic single use • RR of hospitalisation: ✓ 1.10 (range; 1.06 to 1.15) for any method of haemodialyser reuse versus synthetic single use ✓ 1.08 (range; 1.03 to 1.14) for patients treated with formaldehyde reuse versus synthetic single use **b. Quality of life** • Average quality of life of haemodialysis patients treated with single-use dialysers and dialyser reuse was equal, as reported in several studies. **c. Direct costs** • Due to controversy in the inclusion and estimation of some cost items in the analysis, the authors hypothesised **four possible scenarios:** ✓ **Scenario 1;** a sample of 320 patients of whom 85% were able to reuse with an average 13.3 reuses, no extra time required of dialysis staff in performing the reuse process, and a construction cost per person of CAN$ 0.71 ✓ **Scenario 2;** as before but the number of reuses was 10 and 10 minutes extra time were required of dialysis staff per run ✓ **Scenario 3;** the same as scenario 1 but the RR of mortality and hospitalisation for reuse versus single use were assumed to be 1 ✓ **Scenario 4;** the same as scenario 2 but the RR of mortality and hospitalisation for reuse versus single use were assumed to be 1 **d. Indirect cost** • Indirect cost were not included in the analysis **e. Estimated benefits used in the economic analysis** • **QALYs** ✓ In scenarios 1 and 2, estimated QALYs: - 1.648 for synthetic single use - 1.644 for heated citric acid reuse - 1.647 for formaldehyde reuse ✓ In scenarios 3 and 4, estimated QALYs: - 1.648 for all options

- **Cost results**

  ✓ **Cost of dialyser:**

  - CAN$ 18 for single-use per patient
  - CAN$ 12.66 to CAN$ 17.68 for heated citric acid reuse
  - CAN$ 15.47 to CAN$ 20.66 for formaldehyde reuse per reuse

  ✓ **Estimated cost per patient over 5 year time horizon:**

  - **Scenario 1;** CAN$ 218,284 for synthetic single use dialyser, CAN$ 217,073 for heated citric acid reuse, and CAN$ 218,467 for formaldehyde reuse
  - **Scenario 2;** CAN$ 218,284 for synthetic single use dialyser, CAN$ 218,321 for heated citric acid reuse, and CAN$ 219,718 for formaldehyde reuse
  - **Scenario 3;** CAN$ 218,284 for synthetic single use dialyser, CAN$ 216,362 for heated citric acid reuse, and CAN$ 217,515 for formaldehyde reuse
  - **Scenario 4;** Can$ 218,284 for synthetic single use dialyser, CAN$ 217,615 for heated citric acid reuse, and CAN$ 218,768 for formaldehyde reuse

f. Incremental cost-utility ratio (single-use versus heated citric acid reuse)

- **In scenario 1;** cost per QALY of single-use synthetic dialyser over heated citric acid reuse was CAN$ 299,739 per QALY
- **In scenario 2;** single use dialyser dominated the other interventions
- **In scenario 3 and 4;** there were small cost-savings with heated citric acid reuse

g. Sensitivity analysis

- The results of the analysis were only sensitive to the estimates used for the cost of heated citric acid reuse (or alternatively, on the cost difference between heated citric acid reuse and single-use dialysers) and the RR of mortality and hospitalisation for heated citric acid reuse.

h. Resource implications

- Considering the best-case scenario for reuse, scenario 3, a 320-patient haemodialysis unit could save CAN$ 236,621 (CAN$ 739 per patient) per year by switching to heated citric acid. This does not take into account the extra costs that a program considering reuse would face if the reuse facility were located in a different site than the dialysis facility. In addition this saving may be more than offset by the extra expenditure resulting from an increased risk of hospitalisation due to haemodialyser reuse.

Authors conclusion:

ESRD programs can incorporate the results of this study based on their individual situations to determine whether haemodialyser reuse is appropriate in their setting.

General comments

Evidence Table : Economic

Question : Is single use dialyser cost-effective compared to reuse dialyser for haemodialysis of patients with end-stage renal disease (ESRD)?

Bibliographic citation	2. Baris E, McGregor M. The reuse of haemodialysers: an assessment of safety and potential savings. CAN MED ASSOC J.1993;148(2):175-183
Study type / Methods	Economic evaluation (cost- minimisation) conducted in Canada. The aim of this study was to evaluate the safety and potential cost savings of haemodialyser reuse. **Data sources:** All English and French articles published from 1960 to 1991 related to haemodialyser reuse (retrieved through MEDLINE search), the indexes of eight North American Journals from 1960 onward, conference proceedings, associations guidelines, and US and Canadian Laws and regulations. **Cost minimisation analysis:** The basic premise of cost minimisation is that the outcomes of the alternative programmes of interest are identical. Compared the direct costs to the health care system of single use and multiple use dialysers. **Considered three situations that involved different combinations**; **(S1)** highest costs (30 patients per reconditioning system and $35 unit cost per haemodialyser), **(S2)** medium costs (40 patients per system and $30 unit cost per haemodialyser), **(S3)** lowest cost (50 patients per system and $25 unit cost per haemodialyser).
LE	
Number of patients & Patient characteristics	Patient on haemodialysis
Intervention	Single use dialyser
Comparison	Reuse dialyser
Length of follow up	
Outcome measures/ Effect size	**Single use dialyser versus reuse dialyser** • Estimated costs of single use and reuse of haemodialysers in Quebec for 1991 by component which include (system, personnel, operation, and haemodialyser) and situations (S1, S2 and S3): ✓ Cost estimates varied between CAN$ 27.79 and CAN$ 38.19 for single use ✓ Cost estimates varied between CAN$ 7.15 and CAN$ 9.11 for each subsequent reuse ✓ On average 5 uses could save about CAN$ 100 ✓ On average 10 uses could save CAN$ 225 ✓ On the assumption of that a patient receiving long-term dialysis undergoes 156 sessions yearly, the total savings resulting from 5 uses would be CAN$ 3,127 (CAN $ 2,576 to CAN$ 3,629) per patient per year
General comments	

Evidence Table : Economic
Question : Is single use dialyser cost-effective compared to reuse dialyser for haemodialysis of patients with end-stage renal disease (ESRD)?

Bibliographic citation	3. Chuang FR, Lee CH, Chang HW, Lee CN, Chen TC, Chuang CH, Chiou TTY, Wu CH, Yang CC, Wang IK. A quality and cost-benefit analysis of dialyser reuse in hemodialysis patients. Ren Fail. 2008;30(5):521-526
Study type / Methods	Economic evaluation (cost- analysis) conducted in Taiwan. The aim of this study was to evaluate the benefits of dialyser reuse for haemodialysis patients, including the cost of haemodialysis treatment and patient's survival. From January 1, 2005 to December 31, 2005, a total of 125,788 successive haemodialysis treatments in 822 patients in Chang Gung Memorial Hospital-Kaohsiung Medical Centre were included in the study. Patients who survived at least one month beyond the first haemodialysis date were selected. Patients were assigned to reuse if the blood flow rate of their arteriovenous fistula was more than 280 ml per minute and if they were non-hepatitis B carriers and with good heart function at the end of three month entry. The number of instances of dialyser reuse or single use in each patient during the 12 months was retrospectively reviewed.
LE	
Number of patients & Patient characteristics	822 patients • 446 in reuse group (54.25%) • 376 in single use group ● Age (mean in years): ✓ Reuse = 53.4 ± 12.1 ✓ Single use = 59.7 ± 12.5, (reuse versus single use, $P < 0.0001$) Significant difference ($P < 0.05$) of reuse versus single use groups for: ● Age groups ● Sex ● Dialysis duration ● Presence of Hep B ● Presence of DM ● Cause of ESRD ● URR, Kt/V, NPCR, ● TAC urea ● Serum albumin ● Haematocrit ● Comorbidity
Intervention	Reuse dialyser: ✓ Hdf-100S (polysulfone Fresenius) ✓ Polyflux-21S (polymide, Gambro) ✓ F-60 (polysulfone, Fresenius) ✓ BS-1.8 (polysulfone, Toray) ● Sterilised with 4% peracetic acid mixture ● Maximum reuse of six times for each hollow fibre
Comparison	Single use dialyser: ✓ Fx-80 (helixone Fresenius) ✓ FB210U (cellulose triacetate, Nipro) ✓ FB-210G (cellulose triacetate, Nipro) ✓ FB-170G (cellulose acetate, Nipro) ✓ BS-1.6H (polymethylmethacrylate, Toray)
Length of follow up	12 months
Outcome measures/ Effect size	**Reuse dialyser versus single use dialyser** • Average times of dialyser reuse was 2.54 in each patient • Total number of incidents of dialyser reuse was 69,576 within one year • Dialyser reuse was performed in 446 patients within 1 year • **Costs analysis:** ✓ Cost of reprocessing US$ 1.92 (NT$ 62.40), comprised of: - costs of reverse osmosis water (US$ 0.06, NT$ 2) - sterilant (US$ 0.74, NT$ 23.9) - technicians (US$ 0.68, NT$ 22.0) - miscellaneous (US$ 0.45, NT$ 14.5) ✓ Cost for single use of each dialyser = US$ 10.01 (NT$ 325.20) ✓ Cost for each use of dialyser reuse = US$ 6.54 (NT$ 212.60) ✓ Annual cost of hollow fibre reduction for reuse [(325.20-212.60) x 69,576 = NT$ 7,834,257.60 (US$ 241,054.08)] ✓ Annual cost of hollow fibre for reuse was reduced by NT$ 17,565.6 (US$ 540.48) per patient per year
General comments	Cost analysis was not robust.

Evidence Table : Economic
Question : Is single use dialyser cost-effective compared to reuse dialyser for haemodialysis of patients with end-stage renal disease (ESRD)?

Bibliographic citation	4. Mitwalli AH, Abed J, Tarif N, Alam A, Al-Wakeel JS, Abu-Aisha H, Memom N, Sulaimani F, Ternate B, Mensah MO. Dialyser reuse impact on dialyser efficiency, patient morbidily and mortality and cost fechceness. Saudi J Kidney Dis Transplant.2001;12(3):305-311
Study type / Methods	Economic evaluation (cost-analysis) conducted in Saudi Arabia. The aim of this study was to evaluate the effect of dialyser reuse on solute clearance, short term morbidity, dialysate leakage of albumin and cost-effectiveness of the procedure. Ten patients on regular haemodialysis for more the six months at the King Khalid University Hospital's Renal Dialysis Unit, Riyadh, Saudi Arabia were randomly selected to participate in the study.
LE	
Number of patients & Patient characteristics	10 patients on regular haemodialysis: - 5 males - 5 females - Aged between 17 to 70 years - Excluded patients who tested positive to HBsAg and anti-hepatitis C and HIV
Intervention	Reuse dialyser ● Renatron Automated Dialyser Reprocessing system with Renalin was used for sterilisation of dialysers
Comparison	
Length of follow up	3 months
Outcome measures/ Effect size	**Reuse dialyser** • During the three months, 66 dialysers were used for 408 sessions of haemodialysis • Mean reuse episodes = 6.2 ± 5.3 per dialyser • Mean maximum reuse = 13.7 ± 8.0 per dialyser • **Cost analysis:** ✓ Cost of dialysers and other consumables including Renalin solution needed for sterilisation and testing and excluding reuse machine, computer system and personnel was 15,107 Saudi Riyals (≈ $ 4,000) for 10 patients over three months period ✓ If we used the same high-flux dialyser without reuse the total cost would have been 32,640 Saudi Riyals ($ 8,700) thus yielding a saving of 52.8%
General comments	Cost analysis was not robust.

Appendix 6
LIST OF EXCLUDED STUDIES

1. Robinson BM, Feldman HI. Dialyzer Reuse and Patient Outcomes: What do we know now? Semin Dial. 2005; 18(3):175-179.

2. Upadhyay A, Sosa MA, Jaber BL. Single-use versus reusable dialysers: The Known Unknowns. Clin J Am Soc Nephrol. 2007;2:1079-1086.

3. Brown C. Current opinion and controversies of dialyser reuse. Saudi J Kidney Dis Transplant.2001;12(3);352-363.

4. NKF KDOQI Guidelines. Clinical Practice Guidelines and Clinical Practice Recommendations 2006 Update. Hemodialysis adequacy. Available at http://www.kidney.org/professionals/kdoqi/guideline_uphd_va/hd_rec5.htm. Accessed on 17/6/2013.

5. Twardowaki ZJ. Dialyzer reuse-Part II: Advantages and disadvantages. Semin Dial.2006;19(3):217-226.

6. Lacson E Jr, Lazarus JM. Dialyzer best practice: single use or reuse. Semin Dial. 2006;19(2):120-128.

7. Twardowaki ZJ. Dialyzer reuse-Part I: Historical perspective. Semin Dial.2006;19(1):41-53.

8. Locatelli F, Martin-Malo A, Hannedouche T et al. Effects of membrane permeability on survival of hemodialysis patients. J Am Soc Nephrol.2009;20(3):645-654.

9. Hakim RM, Held PJ, Stannard DC et al. Effect of dialysis membrane on mortality of chronic hemodialysis patients. Kidney Int.1996;50(2):566-570.

10. Jone KR. Factors associated with hospitalization in a sample of chronic hemodialysis patients.HSR.1991;26(5):671-699.

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