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Single use versus reusable catheters in intermittent catheterisation for treatment of urinary retention: a protocol for a multicentre, prospective, randomised controlled, non-inferiority trial (COMPaRE)

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ABSTRACT

Introduction Chronic urinary retention is a common lower urinary tract disorder, mostly neurogenic or idiopathic in origin. The preferred treatment is clean intermittent urinary self-catheterisation (CISC) four to six times a day. In most European countries, virtually all patients use single use catheters, which is in contrast to several countries where the use of reusable catheters is more common. The available literature on the use of reusable catheters is conflicting and until now, no randomised controlled trial with sufficient power has been performed to investigate if reusable catheters for CISC is as safe as single use catheters.

Methods and analysis We described this protocol for a prospective, randomised controlled non-inferiority trial to investigate if the use of reusable catheters is as safe as single use catheters for CISC patients, measured by symptomatic urinary tract infections (sUTIs). Secondary objectives are adverse events due to a sUTI, urethral damage, stone formation, quality of life and patient satisfaction. A cost-effectiveness analysis will also be performed. 456 Participants will be randomised into two groups stratified for age, gender, menopausal status and (non-)neurogenic underlying disorder. The intervention group will replace the reusable catheter set every 2 weeks for a new set and replace the cleaning solution every 24 hours. The control group continues to use its own catheters. The primary outcome (amount of sUTIs from baseline to 1 year) will be tested for non-inferiority. Categorical outcome measures will be analysed using χ^2 tests and quantitative outcome variables by t-tests or Mann-Whitney U tests. Two-sided p values will be calculated.

Ethics and dissemination This protocol was reviewed and approved by the Medical Ethics Committee of the Erasmus MC (MEC 2019-0134) and will be performed according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist for non-inferiority trials. The results of this randomised controlled non-inferiority trial will be published in a peer-reviewed journal and will be publicly available.

Trial registration number NL8296.

Strengths and limitations of this study

- This protocol describes a prospective, randomised controlled, non-inferiority study and will provide information regarding the safety, effectiveness, patient satisfaction and costs-effectiveness of reusable catheters in comparison to single use catheters in patients on clean intermittent urinary self-catheterisation (CISC) of the urinary bladder.
- It is the first study protocol with a sufficient sample size calculation able to detect non-inferiority for the reusable catheter measured by symptomatic urinary tract infections (sUTIs).
- The definition of an sUTI is fully and clearly defined in this protocol.
- The steps involved in using the reusable catheter set are more time consuming. This might result in a higher dropout rate in the intervention arm.
- Non-inferiority of the reusable catheter for sUTIs has the following implications: increased patients choice and reducing fear of running out of catheters, a reduction in healthcare costs and plastic medical waste and the opportunity for patients in low income countries to perform CISC with a reusable catheter as the single use catheter at present is much too expensive for the healthcare systems in low-income countries.

BACKGROUND

Millions of people have difficulty in emptying their urinary bladder resulting in urinary retention or clinically significant post void residue (PVR).[1] Urinary retention or significant urinary residue is due to lower urinary tract dysfunction, which can be caused by well-known neurological diseases like spinal cord injury (SCI) or multiple sclerosis, or in some cases it can be idiopathic. To empty the bladder, the treatment of choice is clean intermittent self-catheterisation (CISC) or,

clinically less preferred, an indwelling catheter. Patients administer CISC usually 4–6 times a day, keeping the catheterised volume preferably below 400–500 mL.[2 3] In the Netherlands, virtually all patients on CISC use single use (=disposable) catheters, which is in contrast to several high income non-European countries like Japan, Canada and Australia.[4 5] In those countries, single use and reusable catheters are both used for CISC.

Due to exponential population growth, there is an ongoing increase in healthcare use, and the consequential rising costs and environmental waste are a widespread concern. The global urinary catheter market size was valued at US$4.65 billion in 2020, with gradual growth in future perspective. The majority of this market is formed by intermittent single use catheters, which are accountable for around 60% of the market.[6] The use of disposable catheters in the Netherlands increased substantially in the past two decades from 15 000 users to 46 000 users, resulting in an expenditure of 74 million euros in 2018.[7] The rising costs and environmental pollution are reasons to reduce the use of disposable catheters. Reusable catheters could be a potential cost and waste reduction opportunity.

Other possible advantages of the reusable catheters include increased patient choice and reducing fear of running out of catheters. Several healthcare insurances, provide up to four catheters a day, which is often not sufficient for the needs of all patients. This potentially introduces stress for the patients due to fear of not having enough catheters and does not stimulate the quality of life (QoL) of patients. Additionally, it is clear that storage of large amounts of catheters, or travelling with a stock of catheters, is not ideal for patients.

The current guideline of the European Association of Urology Nurses on intermittent catheterisation discusses the possible advantage in favour of the single use catheters based on low (grade 4) level of evidence, mainly concerning the efficacy of cleaning catheters by different methods.[8] Other guidelines from the European Urology Association (EAU) and the Dutch society for geriatric specialists (Verenso) do not discuss differences between single use and reusable catheters for CISC.[3 9]

The available literature on the differences in safety and efficacy between single use and reusable catheters is conflicting and of low level of evidence. On the one hand, it has been suggested that reuse of catheters introduces unwanted bacterial contamination and therefore increases the risk of symptomatic urinary tract infections (sUTIs) and other complications, like stone formation and urethral strictures.[10] On the other hand, evidence in patients on CISC suggest that reusable catheters are as safe and effective as single use catheters.[11] Prieto *et al* reported in their Cochrane analysis of 2021 that they are uncertain whether there is any difference between single use and multiple-use catheters in the risk of sUTIs because the certainty of the evidence is low.[12 13] Consultant physicians are willing to prescribe reusable catheters or a mixture of single use and reusable, if the use is substantiated by evidence.[14] In view of the lack of this evidence, clinical research is recommended to investigate if the use of reusable catheters are not less safe than single use catheters.[4 11] We designed this randomised controlled non-inferiority trial to answer this question.

METHODS AND DESIGN

Trial design and location

This is a multicentre randomised non-inferiority trial, conducted at the urological department of the Erasmus Medical Center (Erasmus MC) in Rotterdam and the following participating Dutch centres: Amphia Hospital in Breda, Franciscus Gasthuis & Vlietland in Rotterdam, Isala Hospital in Zwolle, Treant Care Group in Emmen and Zuyderland Hospital in Heerlen.

Study population

A total of 456 patients will be recruited for this trial. Patients will be included at the outpatient clinic of the urology department of the participating centres. Patients are found eligible if they are ≥16 years of age and are diagnosed with urinary retention or significant PVR due

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
► Expected chronic, but at least for a duration of twelve months, necessity for daily drainage of the urinary bladder ► Be able to administer CISC via the urethra ≥two times per day and have at least 2 weeks of experience in CISC	► Temporary use of catheterisation because of transient causes ► Known significant urethral stricture which prevents CISC ► Urinary tract stones ► Bladder augmentation ► Non-urethral catheterisation ► History of bladder cancer with active follow-up ► The use of immunosuppressives for transplantation or autoimmune diseases ► Neurocognitive disease which prevents complete comprehension of the study

CISC, clean intermittent urinary self-catheterisation.

to non-neurogenic or neurogenic causes. Further inclusion and exclusion criteria are shown in table 1.

Recruitment

Participants will be recruited at the urological departments of the participating study sites. Patients visiting the hospital will be screened for eligibility and asked if they are willing to receive information on the trial. Patients who are interested to participate will be informed about the study design and the use of the Cliny and PureCath products. First, patients receive an explanation by telephone about the study design and the reusable catheter. If patients are still interested, a comprehensive patient information folder and an instruction video of the reusable catheter will be sent by email to all eligible patients. Patients will be given a minimum of 1 week to consider participation. When a patient decides to participate, a clinical visit is scheduled to demonstrate the reusable catheters. During this visit, the catheters will be demonstrated and it will be checked if the patient has understood all information. If the researcher (M.D. or research nurse) is convinced that the patient understands what participation entails, they will proceed to signing the informed consent form (see online supplemental file 1).

Randomisation

Randomisation is done by the tool ALEA (meaning 'dice' in Latin), according to the regulations of the Erasmus MC. ALEA is developed for randomisation and guarantees concealed allocation. The intervention and control group will be stratified for the participating centres, neurogenic and non-neurogenic causes for catheterisation, age (16–17 years vs ≥18 years and <50 years vs ≥50 years old), gender, and the female patient group will be balanced for premenopausal and postmenopausal status. On randomisation, patients will be allocated a unique study subject number in chronologically ascending order for every study site, starting with 1 (eg, Erasmus MC: EMC001). They will be randomised to the intervention arm (reusable catheter) or control arm (single use catheter). There is no prespecified list on randomisation, but each combination of stratification factors will form a combination. Within each combination, ALEA will randomly assign a study arm. The rational for this approach is that it will maximise the probability of assigning a new participant in the study arm with the lowest number of patients. The company for the randomisation procedure is the Clinical Trial Centre (CTC) of the Erasmus MC.

Blinding

Blinding of the study participants and clinical research staff is impossible due to the different appearances and conditions of the disposable catheters and reusable catheters for CISC. The statistician involved, will be blinded for the intervention and control group during the analysis.

Study arms

Patients are allocated to one of the two study arms:

Intervention arm

Patients in the intervention arm will start using the Cliny catheter (males and females) or the PureCath catheter (only females). These reusable catheters can be introduced without lubricant because of a high-quality smooth surface and will be stored in a holder containing a diluted 2% sodium hypochlorite solution, which will be renewed every 24 hours. The 2% sodium hypochlorite solution is diluted with cold tap water (1:80). In this trial, Milton fluid (a product of Procter and Gamble) is used to clean and store the catheter. To reduce the risk of damage from the cleaning solution, the catheter is rinsed with cold tap water prior to each use. Every reusable catheter will be used for 2 weeks. The reusable catheters are Conformité Européenne (CE)-marked which indicates that the manufacturer confirms the product's compliance with European Union legislation for medical devices (Regulation 2017/745). The manufacturer of the reusable catheter tested the compatibility of cleaning solution with the reusable catheters and recommended the use of 0.6% dilution of 2% sodium hypochlorite w/w solution as cleaning method.

Control arm

Patients allocated to the control arm will remain using their own (single use) catheter, the choice of the single use catheter will be determined by the preference of the patient.

If a study participant no longer requires or is no longer able to safely self-catheterise, the study participation will be terminated and registered as a dropout.

Trial objectives and hypothesis

The primary aim of this trial is to compare single use versus reusable catheters in patients on CISC and to find out if reusing catheters is as safe as the current single use practice, leading to the following primary objective: to determine whether reusable catheters are as safe as single use catheters, measured by sUTIs.

Our secondary objectives are to investigate the safety, efficiency and costs-effectiveness of the reusable catheter and to explore patient opinions on the reusable catheter. Table 2 provides an overview of all objectives and outcome measures.

Our hypothesis is that reusable catheters are as safe and efficient as single use catheters and will provide a significant reduction in healthcare costs and medical waste.

Follow-up and study procedures

During the baseline visit, patients are randomised to one of the two study arms and baseline characteristics including a urine specimen for urine culture are collected. After the baseline visit, participants have 1 week to fill in the first questionnaires before the start of the follow-up period (figure 1). The reusable catheters are ordered and delivered at the home of the study participants who are randomised into the intervention arm. After this week, the intervention arm starts with the use

Table 2 Overview of all objectives and outcome measures

Objectives	Primary outcome	Secondary outcome	Measured by
Safety To determine whether reusable catheters are at least not less safe as single use catheters	No of sUTIs	► Hospitalisation due to a sUTI ► Bacteraemic UTI ► Urethral damage leading to clinical significant strictures ► Kidney/bladder stone formation ► Episodes of macroscopic haematuria	► sUTI (see definition) ► sUTI +hospitalisation records ► sUTI +positive blood culture ► Anamnestic ► Anamnestic ► Anamnestic
Efficiency To investigate whether reusable catheters are not less efficient as single use catheters	X	► Patient satisfaction ► Quality of life	► PROMs: ISCQ, InCaSaQ, PGI-I ► PROM: EQ-5D-5L
Costs-effectiveness To investigate whether reusable catheters are costs-effective in comparison to single use catheters	X	► Quality-adjusted-life-years and incremental costs-effecitiveness ratios	► Hospital records ► PROMs: iMCQ, iPCQ, EQ-5D-5L
Patient opinions To explore patients opinions on healthcare costs and environmental burden in the context of CISC	X	► Patient opinion	► Two statement questions answered by a Likert-scale from 1 to 5 (fully agree – fully disagree)

CISC, clean intermittent urinary self-catheterisation; EQ-5D-5L, Euroqol 5 Dimensional 5 Level; iMCQ, iMTA Medical Consumption Questionnaire; InCaSaQ, Intermittent Catheterisation Satisfaction Questionnaire; iPCQ, iMTA Productivity Costs Questionnaire; ISCQ, Intermittent Self-Catheterisation Questionnaire; PGI-I, Patient Global Impression of Improvement; PROMs, patient-reported outcome measurements; sUTI, symptomatic urinary tract infection.

of the reusable catheters. One year follow-up will be performed according to the schedule.

Primary outcome measure

The main outcome parameters are sUTIs. The definition of a sUTI used for this trial is based on the criteria of Woodford and George, on the basis of the EAU guidelines on Neurourology and the NHG Guidelines for Dutch general practitioners.[3 15 16]

Symptomatic UTI

Patient must meet 1 and 2 below:

1. An acute onset of one or more of the following symptoms:
   - Dysuria/pain during catheterisation
   - Haematuria
   - Urinary frequency
   - Urinary urgency
   - Suprapubic pain
   - Flank pain
   - Fever (>38°C)
   - Rigours
   - Delirium
   - In case of a neurogenic bladder: a change in specific symptoms, like increased urinary incontinence, limb spasm and autonomic dysregulation, could be indicative for a sUTI.
2. And one of the following positive diagnostic tests
   - Positive urine culture
   - Positive dipslide
   - Positive nitrite test
   - Positive urine sediment

If a study participant has a symptomatic UTI, a urine culture will be performed. Based on this result, antibiotics will be started. If a study participant has consulted their general practitioner for a symptomatic UTI, it is possible that antibiotics were started empirically or based on the results of a recent urine culture. The diagnosis is then to be decided by the local consultant involved in study.

Secondary outcome measures

An overview of all outcome measures is provided in table 2. Other parameters such as patients characteristics, possible changes in urine cultures over time, underlying (immune)diseases, hand function and mobility will be assessed as well.

Secondary safety outcome measures

The following secondary outcome measures are used to investigate the safety of the reusable catheters: the amount of bacteraemic UTI (bUTI), hospitalisations due to sUTI, urethral damage leading to clinical significant strictures, clinical significant kidney and/or bladder stone formation and episodes of macroscopic haematuria.

bUTI is defined as a patient with a sUTI and a blood culture positive for a known uropathogen, providing that their urine culture matches the positive blood culture

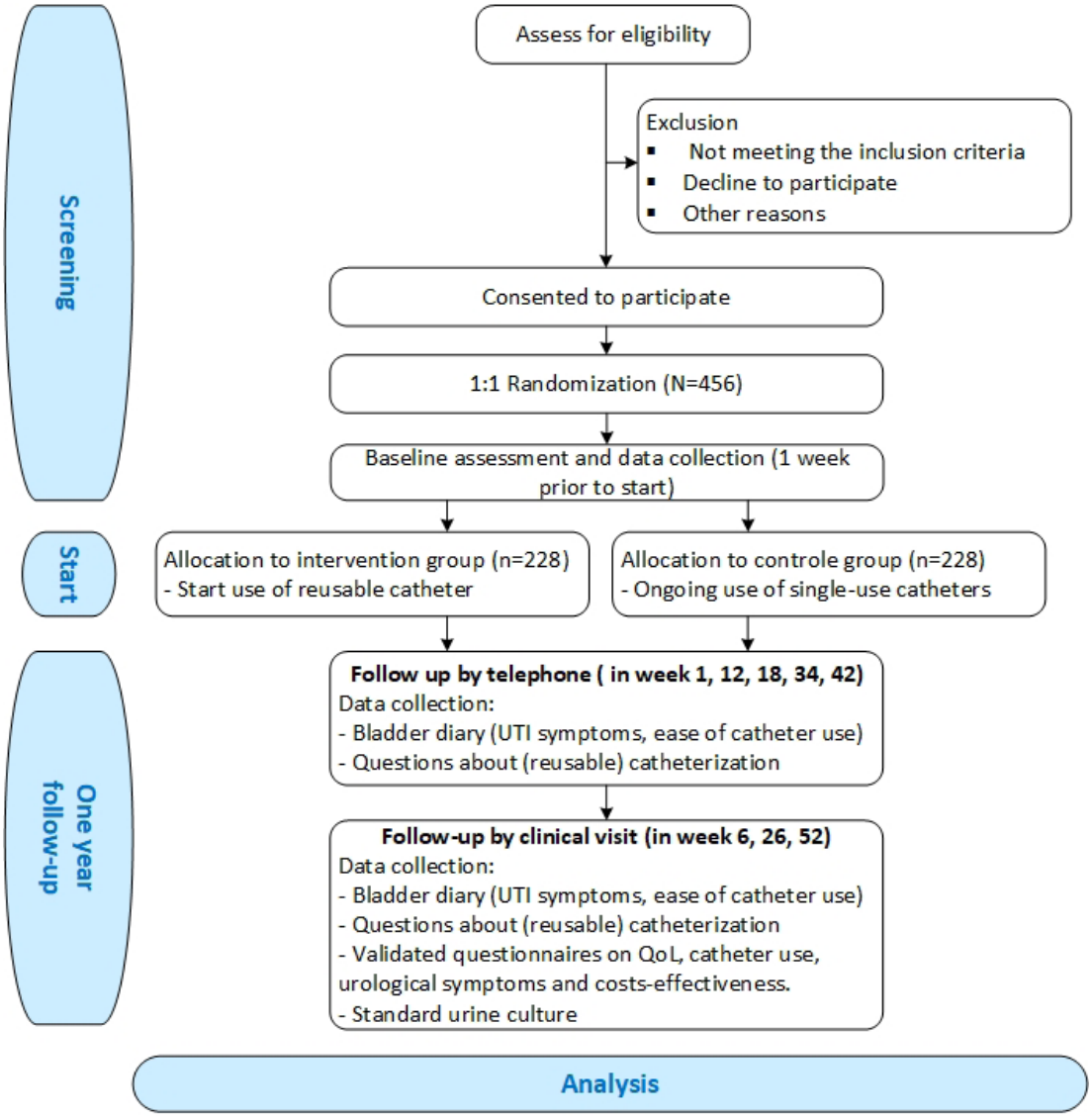

Figure 1 Flow chart of screening and follow-up schedule. QOL, quality of life; UTI symptoms, urinary tract infection symptoms.

(in case a urine culture was taken before receiving antibiotics).

QoL and patient satisfaction in study participants

Patient satisfaction and QoL in the intervention arm will be analysed by multiple validated patient reported outcome measurements (PROMs) relative to baseline (before start of the reusable catheter) and the control group. The following PROMs will be used: the five level version of the Euroqol 5 Dimensional 5 Level, for assessing QoL,[17] the Intermittent Self-Catheterisation Questionnaire, which evaluates QoL in CISC patients, the Intermittent Catheterisation Satisfaction Questionnaire, which evaluates patient satisfaction in CISC patients,[18] and the Patient Global Impression of Improvement.[19] In addition, the Short Form (SF)-Qualiveen, a short-questionnaire measuring urinary specific QoL is used to evaluate urological symptoms.[20] All PROMs will be completed at baseline, weeks 6, 26 and 52.

Patients opinions

Two additional questions concerning patients thoughts on environmental burden and healthcare costs will be asked at baseline and week 52.

Cost-effectiveness analysis

For the purpose of assessing the cost-effectiveness of reusable catheters data will be collected on medical healthcare utilisation, productivity losses and QoL of patients alongside the clinical trial. In this cost-effectiveness study, incremental costs and incremental effects of reusable catheters over single use catheters will be assessed, with effects expressed in quality-adjusted life-years (QALYs). The cost-effectiveness study will adhere to the Dutch health economic guidelines[21] and will be performed by the institute for Medical Technology Assessment (iMTA) of the Erasmus University in Rotterdam. As such the societal perspective will be adopted, meaning that all costs and effects will be included in the analysis,

regardless to whom they accrue. The time horizon of the cost-effectiveness study will be equal to the timeframe of the clinical trial. Uncertainty concerning the incremental cost-effectiveness ratios, QALYs and costs will be assessed using bootstrapping, and this uncertainty will be presented graphically with the CE-acceptability curve. Data on medical healthcare utilisation (ie, volumes) will be collected both through hospital records and by means of the iMTA Medical Consumption Questionnaire.[22] Data on productivity losses will be collected by means of the iMTA Productivity Costs Questionnaire.[23] We will use a willingness to pay (WTP) threshold of €20 000/QALY, based on the reference value for cost-effectiveness determined by the National Healthcare Institute of The Netherlands.[21] A study on health-economic burden of urinary-catheter-associated infection in England used a similar WTP threshold of £20 000/QALY based on the National Institute for Health and Care Excellence guidelines.[24 25]

Sample size

The number of studies that have investigated the effects of single use and reusable catheters is limited. Nevertheless, recently Prieto *et al* performed an abridged Cochrane review.[26] They reported eight studies that compared single to reusable catheters. For single use 44 events out of 199 were observed, for reusable 44 events out of 191. This leads to the proportions of 0.22 and 0.23. Further we applied a power of 0.80, a one-sided alpha of 0.025 (it is customary to adjust one-sided alphas to the half of 0.05) and a non-inferiority margin of 50% of the mean proportions; 0.11, as is recommended by Althunian *et al*.[27] The sample size is then calculated with: $n=((Z(1a)+Z(1-ß))^2\ [ps\ (1-ps)+pe\ (1-pe)])/((ps-pe-d)^2)$, the formula developed by Blackwelder,[28] leading to 182.4 effective cases in each group. Anticipating a dropout of 20%,[29] this must be divided by 80% and rounded upwards. This results in 2 times 228 participants, a total of 456.

Because the lack of comparable non-inferiority designed trials on reusable catheters for CISC with the same primary outcome measurement (sUTI), we chose to look at other non-inferiority trials with a primary outcome measurement of sUTI in patients on CISC. All these trials handled a non-inferiority marge of 10%,[30–34] and two trials even 15%.[35 36] The head researchers and clinicians of the departments of urology and medical microbiology agreed on the 11% marge to be clinical acceptable.

Data collection and management

Data are collected and managed by the (site) researchers in Gemstracker/Limesurvey according to the regulations of the Erasmus MC and the Dutch privacy Law. (Site) investigators will supervise the day-to-day operation of the project and are responsible for ensuring that the Good Clinical Practice guidelines are followed.

Statistical analysis

For analysis of the results, the groups will be stratified for gender and the female patient group will be balanced for premenopausal and postmenopausal. Data analysis will be performed using R (version 4.1.0). The primary analysis will be to assess difference between the intervention and the control groups in the sUTI rate using a risk difference and 95% to determine non-superiority. Descriptive statistics will be used to describe baseline characteristics of participating patients in both groups. Binomial of categorical outcome measures will be analysed using χ^2 tests and quantitative outcome variables by t-tests or Mann-Whitney U tests. Two-sided p values are calculated.

Patient and public involvement

This study protocol was designed with the help of patients who administer CISC. Several patients with chronic CISC have assessed the reusable catheter set by examining and holding it in detail. The research group was advised in the follow-up design, outcome measurements that are important to patients and the practical aspects of the use of this specially designed reusable catheter set. A member of the Dutch patient advocate group for SCI (DON, Dwarslaesie Organisatie Nederland) was also part of the project-group who wrote the funding application. Patients will be involved and consulted on the best way to implement the results of this study in order to guarantee that future adherence will be high.

Monitoring

Monitoring will be done according to the requirements of the Netherlands Federation of University Medical Centres based on the ICH Good Clinical Practice guidelines. Monitoring will be carried out by qualified monitors of the Clinical trial center of the Erasmus MC. The frequency of complications due to participation in this trial are expected to be low and of low severity and not more often or severe than in the general population. Therefore, the Medical Ethical committee of the Erasmus MC classified this study as a low-risk study. For low-risk clinical trials monitoring will comprise one visit per study site per year.

All adverse events will be registered and classified according to the Common Terminology Criteria for Adverse Events published by the National Institutes of Health of the United States of America.[37] In case of a serious adverse event (grade 3 or more), this will be reported to the testing authorities (ToetsingOnline). ToetsingOnline are in control to decide if an early interim analysis is needed to ensure the safety of this trial.

DISCUSSION

Up to now, no randomised controlled trials with sufficient power have been performed to investigate if the use of reusable catheters for CISC is safe and effective in comparison to single use catheters. Only a small number of studies have been performed after the Cochrane

analysis of Prieto et al in 2014.[26 38–41] These studies did not describe whether a proper cleaning technique was used or if the reused catheter was designed for multiple uses. But most of all, no study obtained an adequate sample size to answer the research question. Therefore, the study described in this protocol will add new insights in the use of reusable catheters and provide high-quality evidence if the sample size is achieved (N=456). However, obtaining the sample size might be a pitfall due to following reason: patients who are randomised into the intervention arm need to use the reusable catheter for a year. The reusable catheter is more time consuming due to the preparation measures for safe use. This could potentially result in higher dropout rate in the intervention arm. To minimise the dropout rate, patients are allowed to use a single use catheter in case of emergency. We, therefore, drafted the following rule to minimise any non-compliance in the intervention group: a maximum of 20% of the catheterisations per week may be performed with a disposable catheter. All study participants in the intervention group will be frequently asked if and how often they used disposable catheters. We chose a maximum of 20% so patients who catheterize six times a day are a allowed to use one disposable catheter per day, for example, during the night.

Only a rough estimation can be made about catheter consumption and the plastic waste generated by this, because it is unclear how many people are dependent on chronic CISC. A recent study explored the use of disposable catheters in the Dutch outpatient setting, revealing a prevalence of almost 46 000 chronic and short-term users in 2018 with an expenditure of 74 million euro.[7] Extremely high in comparison to the expenditure of indwelling catheters in the Dutch outpatient setting (only 6,7 million euro for 54 000 users).[42] Almost 25% of the users had a neurogenic underlying disease, which are usually chronic users with multiple[4–6] catheterisations per day. Based on this assumption, the amount of disposable catheters used on an annual basis for users with a neurogenic underlying disease is more than 20 million disposable catheters a year. If the Dutch neurogenic bladder population only uses reusable catheters, this number could be reduced considerably annually depending on frequency of replacement of the reusable catheter, which is in Japan once per 6 weeks and in China once per 12 weeks.

If the outcome of this trial leads to a confirmation of non-inferiority of the reusable catheter in comparison to single use catheters, clinical practice will improve and lead to a reduction in healthcare costs and plastic medical waste in European countries and, ultimately, in the whole world. As a consequence, CISC will also be available in low income countries where the single use catheter at present is much too expensive for the healthcare system.

TRIAL STATUS

Currently, the trial is in the recruitment phase.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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Subject information sheet
COMPaRE

Supplementary 1: Subject informed consent form

"The reuse of catheters in patients who catheterize intermittently"

- I have read the information sheet. I was able to ask questions. My questions have been answered well enough. I had enough time to decide if I want to participate.
- I know that taking part is voluntary. I also know that I can decide at any time not to participate or to stop the study. I do not have to explain why.
- I give consent to inform the general practitioner/specialist(s) who treats me that I am participating in this study and that I will potentially use a reusable catheter.
- I give consent to request information from my general practitioner/specialist(s) about the results from urine analysis and side effects.
- I give consent to request information from the laboratory where the urine analyses were performed.
- I give consent to collect and use my data and body material to answer the research question of this study.
- I know that for the monitoring of this research some people can get access to all my data. These people are listed in this information sheet. I give consent for access by these people.

- I give consent to keep my personal information for a period of 15 years and to use it for future research in the field of my condition and/or the investigated treatment method.

  □ **Yes**

  □ **No**

- I give consent to have my body material stored after this study for use in other research, as stated in the information sheet.

  □ **Yes**

  □ **No**

- I give consent to ask me after this study if I want to participate in a follow-up study.

  □ **Yes**

  □ **No**

- I want to participate in this study.

Name of the subject:

Signature: Date : __ / __ / __

I declare that I have fully informed this subject about the above study.

If any information becomes known during the study that could influence the subject's consent, I will let them know in good time.

Investigator name (or their representative):
Signature: Date: __ / __ / __

Additional information was given by:
Name:
Job title:
Signature: Date: __ / __ / __

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* Delete what is not applicable.

The subject will receive a complete information sheet, together with a signed version of the consent form.