Høgskulen på Vestlandet

Masteroppgave

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Antall ord *:	11709

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Jeg bekrefter at jeg har registrert oppgavetittelen på norsk og engelsk i StudentWeb og vet at denne vil stå på vitnemålet mitt *:	Ja		

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Gruppenavn:	(Anonymisert)
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Andre medlemmer i gruppen:	409

Jeg godkjenner avtalen om publisering av masteroppgaven min *

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Er masteroppgaven skrevet som del av et større forskningsprosjekt ved HVL? *

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Høgskulen på Vestlandet

MASTER THESIS

The effect and safety of subcutanous fluid therapy versus intravenous fluid therapy in the elderly people in nursing homes: a systematic review

Effekt av subkutan væskebehandling på dehydrering hos eldre i sykehjem, sammenliknet med intravenøs væskebehandling: En systematisk oversikt

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Preface

Four years ago we started our master's degree in evidence-based practice at the Western University of Applied Science in Bergen. Evidence-based practice is a conscientious, problem-solving approach to clinical practice that incorporates the best evidence from well-designed studies, patient values and preferences, and a clinician's expertise in making decisions about a patient's care.

We wanted to use our expertise as nurses on a topic we had some experience from, but lacked knowledge from the newest research on the topic. We therefore decided that summarizing available research on the topic for our master's project would be interesting for us as professionals and for our workplace.

Many people deserve to be thanked for making it possible for us to carry out this project. First and foremost, our closest family and our best friends. They have given us respite and patiently endured that most of our time and attention has been about the study.

Many thanks to all our fellow students and in particular to Eva Marie-Louise Denison and Hans Lund, our supervisors. Through their extensive professional knowledge, safe guidance and optimistic feedback, they have always given us the belief that it has been possible to get through with the project.

May, 2021

Gro Holmelid

Laila Hauge

Abstract

This master thesis consists of two parts, an introduction, and a systematic review article. The introduction describes the background of our review question, methods used, and our decisions made along the way in undertaking a systematic review.

Background

Dehydration in the elderly in nursing homes is a problem that the healthcare- professionals must address daily. It`s already a lot of research on the field, but the systematic review findings are of poor quality. We wanted to investigate the effect of subcutaneous fluid therapy in the elderly compared to intravenous fluid therapy and see if there are any new research that will help enlighten our question.

Objectives

The objective of this study is to identify, appraise and synthesize studies examining the effect of interventions of fluid therapy in the elderly population in nursing homes. The research question is “What is the effect of subcutaneous fluid therapy versus intravenous fluid therapy on dehydration in elderly people in nursing homes?”

Methods

A systematic review and meta-analysis were conducted. Systematic search for randomised clinical trials was conducted via the databases of the following platforms: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL and Epistemonikos in April 2020. Two reviewer authors (LH and GH) independently performed study selection, data extraction and risk of bias assessment with the Cochrane Collaborations tools and resources.

Results

A total number of 5595 studies were found after conducting a literature search. After 740 duplicates were removed, we screened title and abstract of 4855 studies. 26 full-text studies were assessed for eligibility. 21 studies were excluded and in the end, we included 3 randomised conrolled trials in this systematic review.

The quality of the included studies were low or had some concerns or high risk of bias. The results indicate a small beneficial effect towards subcutaneous fluid therapy.

Author’s conclusions

The small number of included studies, their heterogeneity and low methodological quality inhibits any firm conclusions on the effects of subcutaneous fluid therapy versus intravenous fluid therapy on dehydration in elderly people in nursing homes. The results indicate a small effect towards subcutaneous fluid therapy compared to intravenous fluid therapy, but the result must be interpreted with caution because of the low certainty of evidence.

Keywords: Systematic review, meta- analysis, dehydration, fluid therapy, Hypodermoclysis, subcutaneous, intravenous.

Sammendrag

Denne masteroppgaven består av to deler, en introduksjon og en systematisk gjennomgangsartikkel. Innledningen beskriver bakgrunnen for vårt gjennomgangsspørsmål, metodene som ble brukt, og våre beslutninger som ble tatt underveis i en systematisk gjennomgang.

Bakgrunn

Dehydrering hos eldre på sykehjem er et problem som helsepersonell må forholde seg til daglig. Det er allerede mye forskning på feltet, men de systematiske oversiktene er av dårlig kvalitet. Vi ønsket å undersøke effekten av subkutan væskebehandling hos eldre sammenlignet med intravenøs væskebehandling og se om det var ny forskning som vil bidra til å belyse spørsmålet vårt.

Mål

Formålet med denne studien er å identifisere, vurdere og syntetisere studier som undersøker effekten av intervensjoner av væsketerapi hos eldre befolkning på sykehjem. Forskningsspørsmålet er "Hva er effekten av subkutan væskebehandling versus intravenøs væskebehandling på dehydrering hos eldre mennesker på sykehjem?"

Metode

En systematisk oversikt og metaanalyse ble gjennomført. Systematisk søk etter randomiserte kliniske studier ble utført via databasene til følgende plattformer: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL og Epistemonikos i april 2020. To anmelderforfattere (LH og GH) utførte uavhengig av hverandre studieseleksjon, dataekstraksjon og risiko for bias med Cochrane Collaborations verktøy og ressurser.

Resultat

Totalt antall 5595 studier ble funnet etter å ha gjennomført et litteratursøk. Etter at 740 duplikater ble fjernet, screenet vi tittel og abstract fra 4855 studier. 26 fulltekststudier ble vurdert for kvalifisering. 22 studier ble ekskludert, og til slutt inkluderte vi 3 randomiserte kontrollerte studier i denne systematiske oversikten. Kvaliteten på de inkluderte studiene var lav eller hadde noen bekymringer eller høy risiko for skjevhet. Resultatene indikerer en liten gunstig effekt mot subkutan væskebehandling.

Forfatterens konklusjoner

Det lave antallet inkluderte studier, deres heterogenitet og lave metodiske kvalitet hemmer eventuelle faste konklusjoner om effekten av subkutan væskebehandling versus intravenøs væskebehandling på dehydrering hos eldre mennesker på sykehjem. Resultatene indikerer en liten effekt mot subkutan væskebehandling sammenlignet med intravenøs væskebehandling, men må tolkes med forsiktighet på grunn av den svake evidensen.

Nøkkelord: Systematisk oversikt, metaanalyse, dehydrering, subkutan, intravenøs, væskebehandling.

Table of contents

1.0 Introduction

Dehydration in the elderly in nursing homes is a problem that healthcare- professionals have to address on a daily basis (Paulis et al., 2018). Due to physiological changes and an increased risk of many diseases the older are more exposed to loss of body water and salt essentials (Thomas et al., 2008; WHO, 2011).

The physiological changes with age leads to a reduced homoestatic capacity and makes the elderly population more susceptible to dehydration (Buffa et al., 2011; Schols et al., 2009; Soiza et al., 2008). The combination of reduced thirst perception and water intake, polypharmacy, cognitive disorders, swallowing malfunction and with kidneys less able to retain water, predispose the elderly to a hydration deficit (Ferry, 2005). Hydration deficits range over a spectrum from minor or asymptomatic to lifethreatening. Concequences as delirium, constipation, renal-infection and insufficiency and severe hypovolemia are common and can reduce quality of life and lead to death (Courtney et al., 2009; Hooper et al., 2014). Appropriate treatment depends on accurately assessing the water deficit and slowly correcting that deficit (Bennett et al., 2004). Increased fluid intake and replacement of lost electrolytes are usually sufficient to restore fluid balances in patients with mild or moderate dehydration. For individuals who are mildly dehydrated, just drinking water may be all the treatment that is needed. The oral route is the choice for hydration because it is easy to perform and non-invasive, but some circumstances (cognitive disturbances, swallowing changes, low level of consciousness, dementia and agitation) , may make it difficult to use this route (Dardaine et al., 1999). When the oral route cannot be instituted, intravenous fluid treatment may be necessary and is most used.

In this case, absorption occurs immediately. However, it is not always possible to administre since the peripheral vessels of the elderly undergo physiological changes typical of aging. It is associated with multiple punctures due to the capillary fragility of the elderly, risk of infection and thrombophlebitis (Ferry, 2005).

To reduce these complications and mainly avoid the numerous attempts of venipuncture, the subcutaneous route has been increasingly used in patients with mild to moderate dehydration.

2.0 Background

2.1 What is subcutaneous fluid therapy (hyperdermoclysis)?

The subcutaneous route has recently begun to regain recognition as a safe, simple and less-expensive alternative to intravenous fluid hydration in mild to moderately dehydrated patients, particularly in long-term care settings. Hypodermoclysis, also known as subcutanous infusion, is an infusion of isotonic fluids into the subcutaneous tissue. When hydrating the patient subcutaneously, a thin needle is put into various sites as the abdomen, thighs and arms. Amounts of fluid infused can range between 1000 ml and 2000 ml over a 24-hour period. Normal saline is the crystalloid most often used (Caccialanza et al., 2018).

2.2 Subcutaneous fluid therapy versus intravenous fluid therapy

Advantages of hypodermoclysis over IV (intravenous) fluids include ease of administration, minimal medical attendance, and no need for hospitalization for administration. It is particularly useful for the elderly patients in the long- time care settings to avoid the danger of admitting patients to hospital. It is also a treatment that is cost-effective. The patient can be treated at site with no need of medical surveillance. In addition, patients admitted in hospital can be discharged at an earlier stage if the only reason for lenghtening the hospital stay is the need for parenteral fluids (Mei & Auerhahn, 2009).

Disadvantages of hyperdermoclysis is that it cannot be used when there is a severe need for fluids (more than 3 liters per 24 hours) at serious dehydration or shock. There are also limitations in the type of electrolyte administration, nutrition additives and medications. Sites of infusion have also been suggested to be changed every 24 hours to reduce local inflammation (Mei & Auerhahn, 2009).

2.3 Critical approch to relevant research on the topic

There have been numerous systematic reviews of effect conducted on this topic, summarized in meta-analyses. In appendix II we show the findings from our critical assessment of these

reviews, most of them comparing hyperdermoclysis to intravenous hydration treatment with the main outcome being laboratory tests of hydration and adverse effects. The main drawback of these studies is methodological shortcomings. The lack of blinding introduces a large risk of bias on the outcomes, as hydrationstatus and adverse effects. Dropouts and switching of interventions also makes the result less trustworthy.

In additon, some of these reviews were from many years back, and we had to consider the possibility of new research on the topic with more valid and reliable results.

When searching the databases and PROSPERO, we came across a protocol from Brasil (Andrade et al., 2017), with a similar research question as ours. Looking further into this we found out that the review were delayed, and it is uncertain if the researchers still work on this project. We have tried to contact them by e-mail, but with no reply. Fellow Head of Centre for Evidence-Based Practice in Bergen University College, Birgitte Graverholt, also tried to contact them without any luck (Appendix III).

We then decided to continue the work with our systematic review.

3.0 Objektives/purpose and research questions

The objective of this study is to conduct a systematic review of the literature, including published and unpublished research, determining the effectiveness of interventions of fluid therapy in the elderly population in nursing homes and the research question is

"What is the effect and safety of subcutaneous fluid therapy versus intravenous fluid therapy on dehydration in elderly people in nursing homes."

The formulation of review question and the methods of the review are based on the Cochrane Handbook for Systematic Reviews of Interventions, which is the official document published by the Cochrane Collaboration detailing the process of conducting a systematic review of healthcare interventions (Higgins & Thomas, 2019).

4.0 Methods

Systematic reviews are the cornerstone of evidence-based medicine and healthcare. They give us the opportunity to combine studies that attemt to answer the same research question, in order to improve consistency of results. They therefore contribute to clinical decision making (Glasziou, 2001, p. 2).

A systematic review answers a defined research question by collecting and summarizing all evidence that fits pre-specified eligibility criteria.

The procedure must be both systematic and explict to limit possible sources of bias and for the work to be verifiable. The Cochrane Collaboration points out that new research only should be design or commissioned if it`s not duplicating already excisting research (Higgins & Thomas, 2019, p. 4).

We decided that a systematic review is the best method to answer our research question.

It is important that the methodology is transparent (Higgins & Thomas, 2019, p. 10). We therefore published a protocol containing the methodological framework. The protocol is approved by our supervisor prior to the start of the review and publiched in Open Science Framework (Hauge & Holmelid, 2020) and available in appendix IV.

The Cochrane Collaboration recommends that a systematic review is conducted by a review team or at least more than one reviewer, in order to minimise the chance of introducing errors into the review process (Higgins & Thomas, 2019, p. 5). Our team consisted of two review authors (LH, GH) and our supervisors.

4.1 Eligibility criteria

Eligibility criteria is based on the PICO elements of the review question and a specification of witch type of studies that have adressed the review question (PICOS). PICOS is an acronym for Population, Intervention, Comparison, Outcome and Study design (Higgins & Thomas, 2019, p. 17). The Population, Intervention, Comparison, Outcomes (PICO) parameters are central to evidence-based research.

The PICOS elements for this review are listed in table 1:

Table 1 PICO

Inclusion criteria	
Population	Elderly population, aged above 65 years, in the setting of nursing homes.
Intervention	The subcutaneous route for the administration of fluids to treat mild to moderate dehydration.
Comparison	The control group is those who receive intravenous fluid therapy, regardless of fluid type, amount and duration of treatment.
Outcome	**Main outcome:** The primary outcome studied will be hydration status. **Measures of effect:** Measured in osmolality, urea, mean arterial pressure (MAP) or other methods. **Additional outcome:** Secondary outcome is to look at complications for the two treatment methods.
Studydesign	Randomised controlled trials
Exclusion criteria	If the studies did not meet the criteria above. Studies were also excluded if they were not reported in the Scandinavian or the English language.

4.1.1 Type of participants

The mean age of the population in nursing homes in Norway is 85 years, see appendix XII (Statistisk_sentralbyrå, 2020).

The geriatric age is defined from 65 years and above and we choose to limit the population from this age in the setting of nursing homes (Den_norske_legeforening, 2011).

We also exclude patients who are dying or with diagnosis that not combine with this treatment.

4.1.2 Types of interventions and comparisons

The subcutaneous route will be compared with the intravenous route for the administration of fluids to treat mild to moderate dehydration in the elderly population, over 65 years, in nursing homes. If there are few studies from nursing homes, we will consider including studies from the hospital settings.

The intervention in this systematic review is those who receive subcutaneous fluid therapy regardless of fluid volume, fluid type and duration of treatment.

The control group is those who receive intravenous fluid therapy, regardless of fluid type, amount, and duration of treatment.

4.1.3 Types of outcome

Based on our study protocol, we divided the many possible outcomes of interest into two categories: primary and secondary outcomes.

The primary outcome studied will be hydration status. Measures of effect: Measured in osmolality, urea, mean arterial pressure (MAP) or other methods.

Secondary outcome is to look at complications for the two treatment methods: adverse effects.

4.1.4 Types of study design

This systematic review has a research question that addresses the effect of an intervention. The randomised controlled trial (RCT) is the most reliable study design to answer these questions.

RCT´s randomly assign participants to different intervention groups, and this is the only way to prevent systematic differences between groups (Higgins & Thomas, 2019, p. 51).

Proper randomisation reduces selection bias at trial entry and is the crucial component of high quality RCTs. Successful randomisation hinges on two steps: generation of an unpredictable allocation sequence and concealment of this sequence from the investigators enrolling participants (Moher et al., 2010).

We decided to include randomised controlled trials that meet our inclusion criteria.

4.2 Litterature search

4.2.1 Search stategies

Our search strategy was developed in multiple steps. First we used the PICO-scheme as a guide to develope a search strategy. The development of the keywords started based on this scheme, together with the inclusion and exclusion criteria. The Cochrane Collaboration recommends that the structure of a search strategy should be based on the main concepts being examined in a review (Higgins & Thomas, 2019, p. 80) This is typically P, population, I, intervention and study design.

We didn´t want to narrow our search by only including our population, elderly above 65 years, in the setting of nursing homes. This because we wanted to identify studies with our population in hospital, in case the results are transferable to our group.

We included different MeSh terms and textwords for dehydration (P) and fluid therapy (I). These terms can differ between databases and are listed in appendix V. The search terms will be adapted for use in the different bibliographic databases in combination with other database-specific filters for randomised controlled trials, where these are available.

The terms were also used in combination with the Boolean operators “AND” and “OR” between each term, and truncation to include all endings ((Lund et al., 2014, pp. 54-58). For instans we truncated the word dehyration, dehydrat* (Appendix V).

In the Cocharane Library we also used the Boolean operator NEXT. We didn´t want to narrow our search by using NOT between terms or including C (comparison) and O (outcome). According to Cochrane Handbook the “NOT” operator should be avoided when it is possible to avoid the danger of inadvertently removing records that are relevant for the search (Higgins & Thomas, 2019, p. 81).

The search strategy aimeds to find both published and unpublished studies. The reference list of all identified reports and articles were searched for additional studies. We had a restriction for English and Scandinavian language, but not any restrictions relating to date of publishing. We re-ran the searches early April 2021, just before the final analyses.

A research libarian peer reviewed our search strategy using Peer Review of Electronic Search Strategies (PRESS). PRESS is a evidence-based checklist to improve the quality of literature searches (Higgins & Thomas, 2019, p. 87) (Appendix V) This is recognized as a necessary step in making a high-quality systematic review. The checklist has six elements in improving the search strategi: 1) translation of the research question, 2) Boolean and proximity operators, 3) subject headings, 4) text word searching, 5) spelling, syntax, and line numbers, and 6) limits and filters (McGowan et al., 2016).

4.2.2 Databases

We conducted a search in different databases chosen with guidance from our supervisor and by recommendations by the Cochrane Handbook (Higgins & Thomas, 2019, pp. 70-74).

Systematic search for randomized clinical trials was conducted via the databases of the following platforms: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL and Epistemonikos.

We also searched the grey literature in Open Grey and conducted a citation search in Web of Science based on the included studies. We didn´t find any new studies.

4.3 Study selection

Before starting on the process of selecting studies, it is important that the reviewers agrees on the characteristics of the eligibility criteria. These are pre-specified.

The study selection is a two step prosess. Firstly, two review authors (LH and GH) independently screened titles and abstract in Covidence based on the inclusion criteria defined in the protocol (i.e. types of studies, participants, and interventions).

Covidence is a web-based software platform for conducting systematic reviews and makes the process much easier for the authors of the review to screen for title and abstract, full text-review, risk of bias assessment and data extraction (Covidence, 2019).

Secondly, we obtained full-text copies of all articles for closer examination. We had to do this in instances where it was difficult to make a selection decision on the basis of the title and abstract alone.

At the full-text level, two authors (LH and GH) independently assessed each identified study for eligibility, resolving any disagreements through discussion with a supervisor.

4.4 Data abstraction

Two review authors (LH and GH) independently extracted data from all eligible studies. We developed the data extraction form, prior data extraction, based on the Cochrane checklist (Higgins 2011, p. 157). We discussed and resolved any discrepancies between us via consensus and with our supervisor. We entered data into Review Manager 5 software (RevMan 5) and recorded study details in the Characteristics of the included studies (and Excluded studies) tables (Revman 5, 2019).

Data that was relevant to retrieve was: Country of study, number of participants in the intervention and control group, dropout rate, outcome measure and age, gender, effect measure and effect estimate. The data retrieval form was piloted by two different people. This helps to ensure data retrieval.

4.5 Risk of bias assessment

The Cochrane risk of bias tool, RoB 2.0 (Lefebvre et al., 2011) , will be used to assess the risk of bias in randomised controlled trials. The evaluation of each trial will be carried out according to the following methodological quality domains: sequence generation, allocation concealment, blinding of participants, personnel and outcomes assessors, incomplete outcome data, selective outcome reporting, and other sources of bias. In this way, the risk of bias for each item will be classified as low, high or uncertain. The risk will be classified as low if all domains are evaluated as appropriate. On the other hand, it will be considered a high risk if one or more of the domains are evaluated as inappropriate or uncertain.

In the capter below we will describe the process of undertaking an assessment using the RoB2 tool.

4.5.1 Domain 1: Bias due to deviations from the randomisation process

Randomised controlled trials comes in a number of variations. Usually the participants are beeing randomised into two groups, the controll group and the intervention group. In some RCT studies, there are more than two groups. You can also have a randomised crossover study when the participants are taking part in both intervention and controll group, but in random order. But «a difficulty with crossover trials, is that there needs to be a credible wash-out period» (Hoffmann, 2017, p. 69). The effects of the intervention must be cleared before the participants are taking part in the controll group. Protocols should describe the planned allocation concealment mechanism in sufficient detail to enable assessment of its adequacy.

The randomisation process is trefolded:

1) Sequence generation
2) Allocation concealment
3) Baseline differences between groups

The randomisation process is the key feature in a RCT study (Hoffmann, 2017, p. 74). We want the participants to be randomly allocated into either an intervention or a controll group. This means that the participants are unaware and can´t control the arm to wich allocated to, and the allocation is referred to as concealed (Higgins & Thomas, 2019, p. 212).

If the process of the randomisation is done correctly the chance of bias are reduced. One bias in this process is "confunding". Then either known og unknown prognostic factors will influence the assignment of individuals to the intervention groups.The randomisation strive to reduce bias by creating groups with similar prognosis. If the treatment decisions are influenced by prognostic factors, for example by recruiting sicker, or less sick, patients to either treatment og control groups, the effect of the intervention will not be trustworthy (Higgins & Thomas, 2019, p. 212). Steps must be made to prevent the recruiting personel from knowing the forthcoming allocations until after recruitment has been done.

There are different methods to ensure a successful randomisation. Blocked randomisation and computer generated allocation.

The randomisation gives no guarantee that the participants in the groups will have similar known baseline characteristics (Hoffmann, 2017, p. 74). It is important that the researcher provides these data so the reader can make up their own mind to whether there is any

imbalance of importance. That is a professional clinical judgement. If the baseline imbalances is of professional importance it can influence the outcomes.(Hoffmann, 2017, p. 74).

This can happen by chance, even if the randomisation process has been carried out correctly. Performing statistical tests for these differences has no value in randomised trials, but it can impact on very small p-values that may indicate a bias in relation to the assigned intervention (Higgins & Thomas, 2019, p. 214).

4.5.2 Domain 2: Bias due to deviations from intended interventions

When using the RoB 2.0 tool to assess the risk of bias in a trial, the review authors need to specify the nature of the effect of interest. The authors must decide if they are interested in the "effect of assignment to intervention" (estimated by an intention-to-treat (ITT) analysis) or the "effect of adhering to intervention" (estimated by an per-protocol-analysis) (Higgins & Thomas, 2019, p. 207).

To preserver the value of the randomisation process it is necessary to use an «intention to treat analysis». This means that the participants assigned to the different groups were assigned even though they did not receive their intended intervention at baseline (Hoffmann, 2017, pp. 79-80). This method can be difficult to carry out, because the data of all participants are needed. Most studies have missing data due to dropouts. The way around this problem is to estimate or imput data statistically to substitute the missing data or «that participants recived the experimental or controll conditions as allocated whitout providing details of what actually done or how missing data were dealt with» (Hoffmann, 2017, p. 80). The reader have to choose to remain sceptical about how this was handled or choose to accept it.

Sometimes the researher choose to estimate the effect of assignment to intervention by using a per-protocol-analysis. This is less valid because the participants are not analysed in the group they were assign to in the begining of the trial. The researcher analyse only the ones that recived the intervention or the control treatment (Lund et al., 2014, p. 112).

In our critical assessment we have to decide if an appropriate analysis was used to estimate the effect of assignment to intervention. We have to look further into if there are dropouts and if all data are accounted for.

This domain is also about blinding/masking of participants, personnel and outcome assessors. Blinding means that the intervention recieved is unknown. This is a necessary step in preventing systematic differences between intervention groups, and researchers should try to blind participants, carers and trial personel, but in some contexts it is difficult to do so. For example in trials comparing surgical with a non-surgical intervention (Higgins & Thomas, 2019, p. 216).

Researchers must rapport if a trial is singel- or doubleblinded. Doubleblinded means that both participants and trial personnel are masked. When singleblinded, only participants are blinded. Blinding of outcome assessors is concidered separately in the «Bias in measurement of the outcome» 4.5.4.

4.5.3 Domain 3: Bias due to missing outcome data:

If the outcome data for some of the participants are missing, the study has bias due to incomplete outcome data. That can occour if the baseline data is incomplete, for example if some of the participants no longer wants to participate or if some of the participants dies during the trial and the reasearcher fails to report back. This will make the effect estimate less reliable. It is important that all the baseline data of the participants is beeing accounted for (Hoffmann, 2017, pp. 74-75). In case of any dropouts, it must be stated how it is treated for outcome measures and in the analysis (Higgins & Thomas, 2019, p. 275). The baseline data is data that describes the participants characteristics, like age, gender and for example measures of the severity of the condition from the pre-testing. Even if the participants have been randomised into different groups, it can be bias in the baseline data that could effect the result of the study (Hoffmann, 2017, pp. 74-75). The professional reader of the study must therefore look for these differences in the groups and use their clinical assessment to make the right judgments in this domain (Hoffmann, 2017, pp. 74-75). Consider, for example, a study about the effect of a pain medication for redusing back pain. If all the participants in one group had more chronic pain at baseline than the other group, the end results of the outcome measured would be doubted if the reaearcher didn´t account for that in the analysis and reported it back to the readers.

It is common in randomised trials to have dropouts. But if the drop out rate are more than 15-20% you must look at the result with caution (Hoffmann, 2017, p. 78). back to the reader

4.5.4 Domain 4: Bias in measurement for the outcome:

To assess whether there is bias in the measurement for the outcome, you need to investigate whether the outcome measured is a subjective or objective measure. «The more objective the outcome that is beiing assessed, the less critical this issue becomes (Hoffmann et al., 2016, p. 76). If it is a subjective measure (pain or quality of life) you need to check if the participants and/or tiral personnel have been blinded through the study. If some of them was not blinded, most likely the outcome measured is biased. They will influence the outcome measure in a negativ or positive direction in relation to their view of the study or in relation to people in the study. In a systematic review (Hoffmann, 2017, pp. 75-77), it was estimated that non-blinded assessors exaggerated the pooled effect size by 68%. If the trial personnel, who are responsible for measuring outcomes, are aware which group the participants are allocated to, they may distort the result by interpret the marginal findings diffrently. Ideally the researcher should report on the success of blinding assessors (Hoffmann, 2017, p. 76). If not the reader will have to speculate about it and then the prosess is not transparent.

4.5.5 Domain 5: Bias in selection of the reported result:

It may be difficult to assess whether there is bias in the reporting of the outcome if there are no protocol to see the article in accordance with (Lund et al., 2014, p. 112). If the protocol is not available, there may be a risk that the authors report the results more positively.

A protocol must state which methods of measurement the researcher plan to use in advance of the study. Then the reader of the article will be able to find out whether all the outcome measures that emerged from the protocol have been reported back on. Or are there any of the results that the researcher has chosen not to report back on? If so, why not. This reporting should be transparent for the reader to find out to avoid publication bias (Lund et al., 2014, p. 112).

4.5.6 Overall bias:

When all domains have been reviewed, the article will receive an overall assessment of the risk of bias. There are three possible outcomes, high, unclear or low risk of bias.
The studies will be considered to have a high risk of bias if one of the mentioned domains has come out with a high risk of bias (Lefebvre et al., 2011).

4.6 Data synthesis

A meta analysis is the statistical process of analyzing and integrate the results from several independent studies. Meta-analyses are often important components of a systematic review procedure. A meta-analysis may be conducted on several clinical trials of a medical treatment, in an effort to obtain a better understanding of how well the treatment works. Here it is convenient to follow the terminology used by the Cochrane Collaboration and the use of the methods outlined in the handbook should provide a consistent approach to the conduct of meta-analysis. (Haidich, 2010).

Before conducting a meta-analysis it must be determined if the studies found are similar enough to be grouped within each comparison (Higgins & Thomas, 2019, p. 232). Tabulating "Characteristics of the included studies" (Attatchment IX) is helpful to explore and compare PICO elements across studies. The next step is to evaluate what kind of data is available for a synthesis and choose the effect measures for comparing intervention groups (Higgins & Thomas, 2019, p. 241).

We used RevMan 5 software to conduct meta-analysis when at least two studies using the same design provided sufficient numerical data on the same outcome (Revman 5, 2019). The result are illustrated by a forest plot.

For continuously measured outcomes, the standardized mean difference between the experimental and control groups was calculated for each study, based on the mean and standard deviation after the treatment, and the number of subjects in the two groups. For the outcome adverce effects we reported number of events.

Due to the different scales used to report hydration status as a continuous outcome, these results are reported as standardised mean differences (SMD). Standarised mean differences are used when we need to summerize the statistic in a meta-analysis, but the same outcome

are measured in different ways. For example there is a variety of ways to measure pain, and different scales are used. In these situations it is possible to standarize the result of the outcome to a uniform scale before they can be combined (Higgins & Thomas, 2019, p. 157).

4.7 Assessing the quality of the evidence

Issues that can affect the quality of the evidence derived from systematic reviews, led to development of the GRADE criteria. The Grades of Recommendation, Assessment, Development and Evaluation Working Group has developed this system and it is the most used approch for grading the certainty of evidence in the effects of interventions by outcome across studies (Guyatt et al., 2008).

The system consists of five considerations: risk of bias, consistency of effect, imprecision, indirectness and publication bias. The software "GRADEpro" was use to rate the result of each outcome and to create a "summary of findings" table.

The level of evidence from RCTs is regarded as high quality, but can be downgraded to moderate, low or very low quality after being evaluated by the GRADE criteria (Higgins & Thomas, 2019, pp. 390-391).

The five domains are described further in this chapter.

4.7.1 Study limitations

Risk of bias or limitations in the design and implementation of available studies:

RCT is regarded as high quality, but methodological limitations will likely lead to a biased assessment of the intervention effect. For randomised controlled trials included in the review, this may be failure in relation to measures of internal validity such as allocation concealment or blinding. There are no objective criteria on which to assign a particular group of included studies as a risk of bias and it is therefore a subjective judgment on the part of the review author (Higgins & Thomas, 2019, p. 392).

4.7.2 Inconsistency of results

Heterogeneity or "inconsistency" is a measure of differences in the estimates of treatment effect across studies. When there is differences in the estimates, the author should look for explanations for this difference in heterogeneity. If authors fail to explain why results may vary from population to population through investigation of heterogeneity, evidence should be downgraded (5.2.2.Schünemann et al., 2013).

The I^2 statistic describes the percentage of variation across studies that is due to heterogeneity rather than chance. The P-value obtained in this analysis expresses the probability that the variation between the effect estimates of the individual studies included in the meta-analysis is not random. This p-value is found on the basis of the Chi2 value and the number of degrees of freedom (Lund et al., 2014, p. 151). When the p-value is less than 0.1, we can reject the hypothesis. A heterogeneity of less than 40% will most likely not effect the result. A heterogeneity between 30-60%, means that it is a moderate. When you reach between 50-90% you have a large to serious heterogeneity (Lund et al., 2014, p. 151).

Unexplained heterogeneity or inconsistency of results: When there is differences in the estimates of treatment effect across studies, the author should look for explanations for this difference in heterogeneity. If authors fail to explain why results may vary from population to population through investigation of heterogeneity, evidence should be downgraded (5.2.2.Schünemann et al., 2013).

4.7.3 Inderectness of evidence.

The Grade handbook explains indirectness like this: “We are more confident in the results when we have direct evidence. Direct evidence consists of research that directly compares the interventions which we are interested in, delivered to the populations in which we are interested, and measures the outcomes important to patient” (5.2.3.Schünemann et al., 2013).

This measure relates to the population, intervention or outcomes measured and whether they are relevant to the population on which the evidence is to be used.

4.7.4 Imprecision of results

If a review includes too few participants or events and/or the confidence interval are very wide, this will result in imprecision and reduced confidence to the result. With a wide CI it includes both an effect in favor of the intervention group and an effect in favor of the control group (Higgins & Thomas, 2019, p. 394).

In this case, the author may judge the quality of the evidence lower than it otherwise would be considered.

4.7.5 Publication bias

Should there be evidence of possible publication bias, and the researcher fail to report studies on the basis of the results, then evidence is downgraded. For example are studies with small sample size more likely to remain unpublished or ignored (Higgins s 394).

5.0 Results

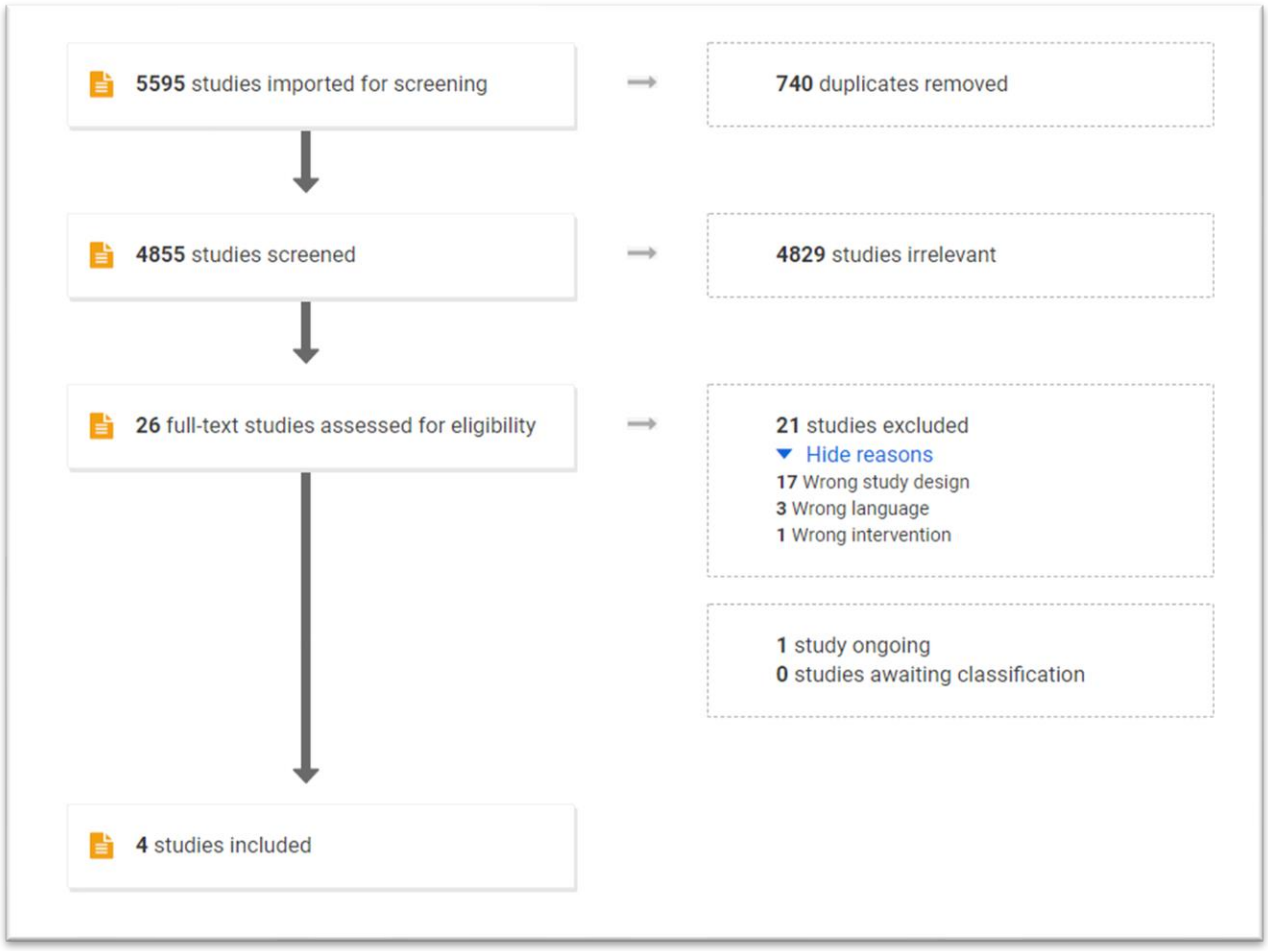
A total numer of 5595 studies were found after conducting a literature search. After 740 duplicates were removed, we screened title and abstact of 4855 studies. 26 full-text studies were assessed for eligibility. 22 studies were excluded and the reason for exclusion is presented in attachment X.

We included 3 RCT‘s.

There were one study with a crossover-design, (Esmeray et al., 2018), that also met our criteria of inclusion. We decided through our dataextraction-process to not include the study afterall, when looking further into the rapporting of the outcome. In the end it wasn`t possible to conduct the data from each intervention separately prior switching of groups, and we couldn`t include the data in our meta-analysis.

The selection of eligible studies was conducted based on the PRISMA 2009 flow diagram (Moher et al., 2009) and the whole selection process is presented in Figure 1

Figure 1: Flow Chart



5.1 Description of the included studies

Description of the included studies is available in attatchment XI.

5.1.1 Study characteristics

We included 3 RCT (Challiner et al., 1994; O'keeffe & Lavan, 1996; Slesak et al., 2003) in our systematic review.

5.1.2 Characteristics of the participants

All three studies included participants aged above 65 years. In all studies the mean age is above 80 years, and the study participants are either from nursing home residents or from geriatric wards in the hospital settings.

The participants of these studies were diagnosed with mild to moderate dehydration, and in need of parenteral fluid substitution.

5.1.3 Intervention and comparator

Attachment XI includes information on the interventions of the included studies. All included studies compared intravenous fluid therapy with subcutaneous fluid therapy, where the control group are those who receive intravenous fluid therapy, regardless of fluid type, amount and duration of treatment.

The duration of treatment varied from 48 hours to 6 days, administred in the same way across the three studies. Subcutaneous fluids were mostly administred through subcutanous tissue in abdomen area, and the intravenous fluid through an IV access.

Half of the patients recieved fluids subcutanously and the other half received fluids through an intravenous canula.

5.1.4 Outcome and outcome measures

The primary outcome, hydrationstatus, were measured differently across the studies. They all measure different blood samples for hydratingstatus, but Slesak (2003) also measures MAP and puls. We only included the varies of bloodsamples that rapported mean and SD in our meta-analysis. Challiner (1994) measures the bloodsample serum osmolalitet and Slesak (2003) serum sodium in these variables.

All three studies rapported adverse effects, our secondary outcome, in number of events, categorized in minor and major adverse effects.

Because of the different measures of hydration, we had our difficulties in aligning these studies with eachother. It`s hard to define dehydration with one symptom alone or an answer from a laboratory test (Thomas et al., 2008). Slesak 2003 conducted five different ways of measure hydration, but we could only choose one of them in our meta-analysis. The methods of measurement used in the study of Slesak to describe hydration status were mean artery pressure (MAP), pulse and three different blood samples (hematocrit, sodium and creatinine). In Challiner 1994, a blood sample, osmolality, was used as the measure of hydration.

Below is a review of the various methods for the outcome measure, hydration status, which have been mentioned above (and why we choose the ones we did):

MAP: MAP indicates how much fluid pressure is inside the arteries / blood vessels. If you have a lot of fluid that circulates in the bloodstream, it indicates that you are well hydrated (Gulbrandsen & Stubberud, 2015, p. 268). There are several mechanisms that can influence MAP. For example, you may have a high MAP pressure if you are given a contracting drug that causes the arteries to contract. Also, the albumin values has a lot of influence of the body in relation to creating an osmotic pressure that helps to draw fluid from cells in the body and into the bloodstream. If you have little of this protein (Albumin), the fluid from the bloodstream can also leak into the tissue and away from the blood vessels. This will result in a low blood pressure and a low MAP. So MAP is not a good measure for mild to moderate dehydration as it usually does not affect blood pressure and it is all these other factors that can also play a role in influencing the outcome measure (Gulbrandsen & Stubberud, 2015, pp. 267-269).

Pulse per minute: Pulse is the rhythmic dilation of an artery that results from beating of the heart. The contraction of the heart pumps blood to the body cells, supporting them with oxygen. At a low blood volume, one of the physiological ways to deliver more oxygen to an organ is to increase heart rate to permit blood to pass by the vital organ more often. Normal resting heart rates range from 60-100 bpm. The heart rate can also be affected by many other factors such as stress, activity, fever and more. So it is not a reliable measure of dehydration alone. However, there may be one sign along with other clinical and objective parameters of dehydration (Almås, 1998, pp. 334-340).

Hematocrit or erythrocyte volume fraction (EVF) can be measured by taking a blood sample. Hematrocrit/EVF is the proportion of the blood volume that is made up of the erythrocyte volume (Hokland & Madsen, 1994, p. 23). When a person is dehydrated and have

less circulating fluid in the bloodstream, the values of EVF will be high. It may be an good indicator of dehydration, but one will need more objective parameters and clinical signs to make the diagnosis.

Creatinine is a waste product that comes from muscle metabolism in the body. Everyone has creatinine in their bloodstream. The level of creatinine in your blood depends on your age, race, gender, and body size With a lage muscle mass, the levels of creatinin can be high. Even though the elderly has a low muscle mass, the serum creatinine concentration usually increases with age. This has to do with poorer renal function with age (Tiao et al., 2002).

Serum creatinine is a measure to assess renal function. S-creatinin can also be high in case of dehydration. As dehydration progresses, the volume of fluid in the body decreases, and blood pressure may fall. This can decrease blood flow to vital organs (as the kidneys), and leads to a malfunction (Tiao et al., 2002). Mild to moderate dehydration do not necessary affect the blood pressure and renal functions, so we have to keep that in mind when assessing this as a measure regarding our review question.

Osmolality and sodium (s-sodium):

The body fluids are drawn in and out of the cells in the body by means of osmotic forces. At a high concentration of salt (sodium) in a cell, an osmotic pressure is created which causes water to diffuse from the cell with a lower salt level and into the cell with the highest concentration to even out the concentration differences in the two cells. Normal osmotic pressure or osmolality is 290 mosmol / kg (Hokland & Madsen, 1994, pp. 49-50). In practice, s-osmolality is rarely used, but instead s-sodium is used to distinguish between the different forms of dehydration, hypoertonic and isotonic dehydration. In hypertonic dehydration, s-sodium is above 148 mmol / l. Hypertonic dehydration occurs when water intake is too low or the body loses low-salt fluid. Common in the elderly with for example low intake of wather, who have a fever or sweats heavily (Hokland & Madsen, 1994, p. 51). Isotonic dehydration gives an s-sodium between 135-148 mmol / l. Common causes are vomiting, diarrhea, bleeding, ileus and asites. In hypotonic dehydration, s-sodium is below 135 mmol / l. Causes of this type can be kidney disease or drug overdose of diuretics (Hokland & Madsen, 1994, pp. 51-52). Older people over the age of 65 may be at risk of getting these types of dehydration. The normal range for s-sodium is between 135-148 mmol / l (Hokland & Madsen, 1994, p. 49), which is the same for isotonic dehydration. To assess whether the patient is dehydrated or not, the clinical signs of the patient are crucial. Based on the fact that we consider sodium to be the

most suitable measure to be able to measure dehydration objectively, we choose to extract this data for our meta-analysis. However, it is important to note that the diagnosis of dehydration is made on a clinical indication by the doctor. Symptoms of dehydration are: thirst, dry mucous membranes, standing skin follicles and weight loss (Hokland & Madsen, 1994).

5.2 Risk of bias assessment in the 3 inkluded studies in the review

With the help of the RoB 2.0 tool (Lefebvre et al., 2011), we critically assessed our three included studies. Details of the risk of bias assessment are available in attatchment XII.

Below is a summary of our critical assessment of the three included studies, based on our two outcome measures, hydration status and adverse effects:

5.2.1 Bias arising from the randomization process

Two of our three includes studies (O'keeffe & Lavan, 1996; Slesak et al., 2003), were judged to have a high risk of bias arising from the randomisation prosess. The studies of O'Keeffe and Slesak reported that the allocation was determined by clinicians after patients had met the inclusion criteria for participation in the study. This is a quasi-random assignment which is an unsuitable allocation method with a high risk of bias as the randomisation of the patients was not completely random cf. section 4.5.1. The assignment to which intervention the participants were allocated to was hidden by the use of a concealed envelope. The participants were then equally divided into the two groups.

Other baseline characteristics in the study of O'keeffe were presented in a table showing the mean age, number of females, how agitated the participants were, and two different blood test for hydration status in the two groups. These data look relatively similar in the two groups and according to our clinical assessment should not have such a large impact on the end result of the study in relation to this.

The study from Slesak had also listed baseline characteristics such as age, gender and various diagnoses among the participants and listed how many had similar diagnoses in both groups. With such similar baseline data in the subcutaneous and intravenous group we considered it

not to affect the result as long as the rest of the study satisfied the other domains. However, having said that, this study already had high bias related to the selection process which indicates that methodically this study already has a high risk of bias.

The third included study (Challiner et al., 1994) is considered to have a low risk on this domain. They reported that they had used block randomization generated by a computer. And the allocation was hidden with sealed envelopes. They also reported baseline numbers with an equal number of 17 participants in each group after randomization. The average age in both groups was not stated in groups, but for all 34 participants in total. Otherwise, there was little information about baseline characteristics from the two groups other than that they reported that: "An analysis of covariance was performed to allow for differences in baseline between groups" (Challiner et al., 1994, p. 1) and that the p-value showed according to themselves: «no statistical difference» between the groups ($p = 0.12$). This means that there is a 12% uncertainty as to whether the differences in measured osmolality in baseline characteristics between the participants in the groups may have affected the result. One would like this uncertainty to be below 5%, ie a p-value of less than 0.05 (Hoffmann, 2017, p. 35). However, as mentioned in section 4.5.1, it is of no value to perform such a test in randomized trials as this study when the randomization process has been performed correctly. We find no evidence to suspect that there is anything wrong with the randomization process in the study of Challiner, but the researchers could have been a little more generous with their reporting to the reader.

5.2.2 Bias tue to deviations from intended interventions

In this domain we needed to assess two topics in the three included studies:

- Assignment to intervention (ITT) or adering to intervention (The per-protocol effect)
- Blinding

The value of conducting a randomised controlled study that will ensure you to trust the results afterwards, is when the analysis is an "intention to treat analysis" cf. section 4.5.2 which is a kind of gold standard for this the method. But it is not always possible in practice, as in our three included studies. In our included studies, there were so-called "dropouts" which resulted in missing data in the final analysis. Our critical assessment therefore concluded that they all had a "per protocol analysis" based on this. Despite the fact that the

study of Sleasak 2003, even reported that they had used an "intention- to- treat analysis" (See Appendix X).

In Slesak 2003, the participants could change groups if there were medical or ethical reasons why the participants needed this. 17 patients switched from i.v. to s.c and 11 patients switched from s.c to i.v. Whether this was planned for or not is difficult to assess since we`re not been able to find the protocol for this study. We consider this to be a high risk of bias as it becomes less transparent for us as readers. The reporting for the final data on adverse effects is unclear whether all participants have been included or not as Table 2 only shows the number of side effects reported after treatment and it is not possible to read how many of the patients have been accounted for.

In O`Keeffe, not all participants have been included in the analysis and the study will then be considered a "per protocol effect". There are two participants with missing outcome data, and this amount are concidered as small. More than 95% of the data presented are available and the missing outcome data will probably not have a significant effect on the result of the study. The domain “Bias due to missing outcome data” for the outcome measure adverce effects, is considered to have a low risk of bias in O`Keffe's (1996) study. The study of Challiner, 1994, was quite similar to O`Keffe with only two dropouts. Thsi is also considered to have a low risk of bias for this domain. (Otherwise see the assessments in appendix X).

In the Sleasak 2003 study, the participants or the trial personell was not blinded for the assigned intervention during the trial. That is impossible in this study, because both participants could see what the treatment they recived and th trial personell needed to see it to administer fluid therapy to the participants. The intervention-group was reciving subcutaneous fluid therapy and the controll-group got intravenous fluid therapy. This is a huge potential for bias in the study that the researchers could not avoid. For the two outcome, hydration status and adverse effects, we assess the last one to be subjective.

The treatment was not blinded in the Challiner 1994 study for the same reason as in Sleasak 2003. We also did not consider any deviation from the intended intervention. The participants got the treatment intended.

5.2.3 Bias due to missing outcome data

In order to avoid bias due to missing outcome data, it is important that there are no missing data when analyzing a result. Dropouts must be reported back and the analysis process must be transparent to the reader how this has been taken into account, cf. 4.5.3.

Regarding our outcome measure, hydration status, we have critically considered two relevant articles, (Challiner et al., 1994; Slesak et al., 2003), and as mentioned above, these have different dropout rates. Slesak has a dropout rate at 23 % for data on the blood sample sodium (shown in Table 3) in their study. Other parameters such as Map, heart rate, hematocrit and creatinine have been used for this outcome measure. None of these methods of measurement for hydration status had all the data for all 48 included participants (Slesak et al., 2003, p. 158). Even in baseline data, data was missing on some of the included participants. Challiner is considered to have a low risk of bias on this domain as they do not lack data for this outcome measure.

When we look at the data for adverse effects in the study of Slesak, only the number of adverse effects are counted for and not how many of the participants this applies to. There are more events of adverse effects than the number of participants, so some of the participants are included more than once. This is an example of a "unit-of-measurement-error" which means that the number of side effects has been measured instead of the number of patients who had experienced the side effects.

Challiner reports two minor local reactions in s.c. group (erythema) and a participant in i.v. the group that got bruising. Otherwise, we consider this study to have an unclear risk of bias due to very little information in the study. Regarding the adverse effect and the study of O`Keffe, we considered a low risk of bias on domain 3, more than 95% of the data were available for analysis.

5.2.4 Bias in measurement of the outcome

For our two outcome measures, hydration status and adverse effects, we had to examine whether the outcome measures were objective or subjective. If we look at hydration status first and the two studies, Sleasak and Challinger that have measured this, they have both measured this outcome in an objective way. Schlesak refers to MAP, heart rate and various

blood tests (hematocrit, sodium and creatinine) while Challiner refers to only one blood test, osmolality. Based on the fact that these are objective measurement methods considered to have less risk of bias associated with this outcome measure, cf. section 4.5.4.

But for outcome measure, adverse effects, it seems to be a subjective. In the study of Slesak it was health personnel who both observed and measured and wrote down the side effects. This is therefore to be regarded as a risk of bias as it is a subjective measurement method that can affect the result. The other two studies that also looked at this, Challiner and O`Keeffe, had a very lack of information on how they had proceeded when measuring these side effects. This lack of reporting here is therefore considered a risk of bias for these studies. Challiner is considered to be an unclear risk and O`keeffe is considered to have a high risk of bias (See appendix X).

5.2.5 Bias in selection of the reported result

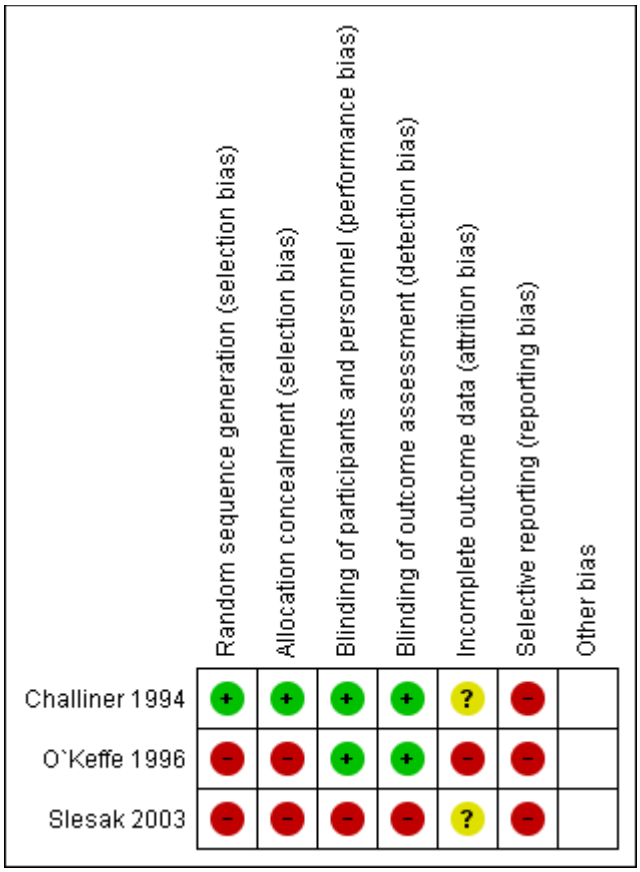
We have not succeeded in finding the protocols for any of the included studies, and there may be a risk that the result will be reported more positively than what was intended in advance, cf. section 4.5.5. All studies are therefore considered to have a high risk of publication bias. (See appendix X).

5.2.6 Summery of risk of bias of included studies

The overall assessment for the 3 included studies have we summed in the figur nr 2 below:

Figur nr 2

Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

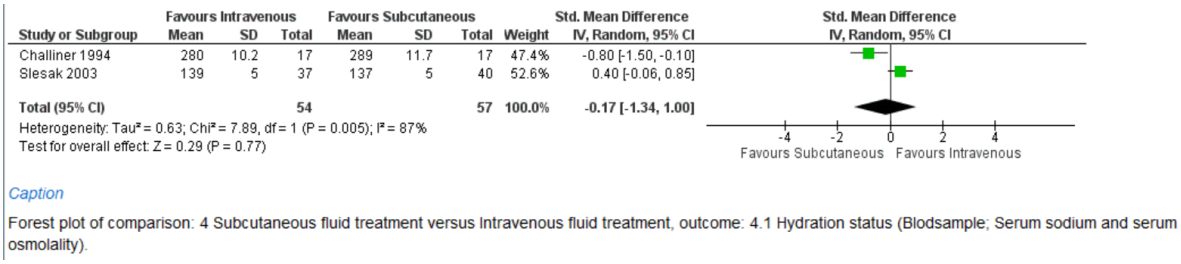


5.3 Effect of intervention

We have analyzed the available data for the included studies in two meta-analyzes using Revman 5 software, cf. section 4.6. For the outcome measure, hydration status, the studies Challiner and Slesak reported data with different measurement methods for the same outcome. Due to the different scales used to report hydration status as a continuous outcome,

these results are reported as standardized mean differences (SMD) cf. point 4.6. From Challiner, we extracted the blood value, osmolality, and compared this with the blood value, sodium, from Slesak after the fluid treatment in the two groups. The result of this analysis is shown in figure 3.

Figur 3



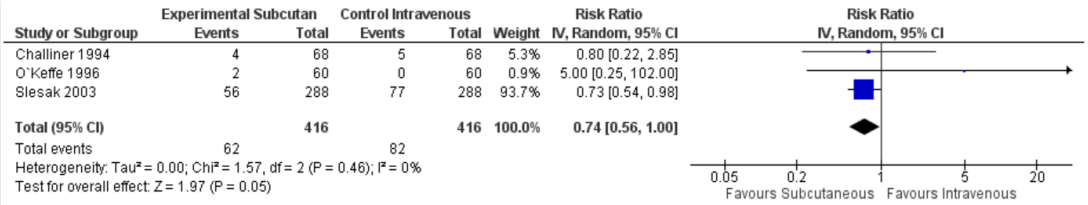
Caption

Forest plot of comparison: 4 Subcutaneous fluid treatment versus Intravenous fluid treatment, outcome: 4.1 Hydration status (Blodsample; Serum sodium and serum osmolality).

The measure of effect from this analysis shows an SMD of 0.17, which means that subcutaneous fluid therapy is favored compared to intravenous fluid therapy. The 95% confidence interval shows -1.34-1.00. Our analysis comes out with a very large heterogeneity (cf. section 4.7.2) of 87% and a p-value of 0.005 which means that there is a high degree of variation between the studies which is not random and which should be explained. Reasons why they are different can be explained by the fact that the hydration status has been measured in different ways in the two studies and that we have too few studies in our analysis for us to get an effect estimate with a lower heterogeneity.

If we look at our second outcome measure, adverse effects, these data were dichotomous and here we had to make an analysis that looked at how many side effects had been reported in the different groups against the number of fluid infusion treatments. For this analysis, we were able to include all three of our studies as they had data on adverse effects. The result of the meta-analysis on this outcome measure is shown in figur 4.

Figur 4



Caption

Forest plot of comparison: Outcome: Adverse effects.

The number of events indicates how many side effects the participants experienced after x number of infusions in subcutaneous group versus intravenous group.

This analysis shows a relative risk (RR) of 0.74, with a 95% confidence interval of 0.56-1.00 favoring the subcutaneous group. The heterogeneity becomes 0% with a p-value of 0.05. This is probably related to the fact that there is one of the studies dominates in this analysis and which is weighted 93.7%. And then it means less that the studies of O`Keeffe and Challiner have broad confidence intervals because it does not affect the result to the same degree as in the analysis above. Overall, we see from the analysis that there is a 26% lower risk of adverce effects with subcutaneous fluid therapy than with intravenous fluid therapy, but we can not conclude that this effect is significant, as we have very few studies in our analysis and there is an uncertainty in whether all studies have had different ways of registering these side effects. There is no information on how this has taken place in O`Keeffe and Challinger, while in Slesak it was nurses and doctors who observed and measured the side effects and wrote them down in a standardized form cf. Appendix X.

5.4 Sensitivity analysis and subgroup analysis

Given the small number of identified studies we were unable to conduct any such subgroup analyses. Based on the nature of the meta-analyses, we could not conduct sensitivity analyses, as each meta-analysis combined only two effect sizes.

5.5 Robustness of the synthesis

Below we review the result of our GRADE assessment, cf. section 4.7. We have been two authors performing this assessment. There has been no disagreement and therefore not necessary to include a third party in our judgment.

5.5.1 Studylimitations

The study design on which a study is based is of great importance for the quality assessment of the result that emerges in a meta-analysis. A randomised controlled trial starts at the highest quality compared to other study designs, cf. section 4.7.1. All of our included studies in our systematic review are randomised controlled trials. The assessment therefore starts at a high quality for both outcome measures. Both studies that were included in our analysis for outcome measure hydration status (Challiner and Sleasak) were considered to have a high risk of bias compared to section 5.2 and Appendix XI. We downgraded one step for this.

For the outcome measure adverse effects, we had three included studies. The study of O`Keeffe was considered to have a high risk of bias together with the study of Slesak. Challiner was considered to have "some concerns" cf. 5.2 and appendix XI. We downgraded one step for this. This downgrade occurs because the internal validity of the included studies is weakened.

5.5.2 Inconsistency of results

If the effect estimates between the different studies are different, the analysis can show a high heterogeneity, cf. section 4.7.2. This means that there is a discrepancy in the results between the studies. This can occur when the results of the included studies in a pooled meta-analysis point in different directions or that there is a large difference in the effect size between the different studies. For the outcome measure hydration status, a heterogeneity / I2 was 87% compared to Figure 3, domain 5.3. and a p-value of 0.005 which may indicate an inconsistency between the studies which is not accidental cf. section 4.7.2 This is explained by the fact that we combined the results from Slesak, which favored intravenous fluid

treatment (effect estimate 0.40 and Confidence interval -0.6 -0.85) against Challiner who favored subcutaneous fluid therapy (effect estimate -0.80 and confidence interval -1.5-0.10). A heterogeneity of more than 75% is considered to be very high (Lund et al., 2014, p. 151) and then gives a downgrade for this outcome measure in our GRADE assessment as this is a very serious inconsistency. This indicates a warning that it may not give a meaningful result when you combine these current studies.

If we look at our second outcome measure, adverse effect, the heterogeneity is 0%. The reason for this is that there is a study here that dominates in size. Slesak's study weighs 93.7% of the total. The other two studies included in the meta-analysis (Figure 4, domain 5.3) are so small that they have no significance for the heterogeneity and the overlapping confidence intervals. The grade assessment here therefore comes out as “not serious” and is not downgraded.

5.5.3 Indirectness of evidence

For both of our outcomes we have considered the directness as “not serious”. This is because our 3 studies have similar study participants, aged above 65 years, and the same intervention, subcutaneous fluid therapy and the same comparison, intravenous fluid therapy. They also have the same outcome measure.

5.5.4 Imprecision

Under this domain we assess the degree of uncertainty and precision inherent in the results of the meta-analysis. The outcome, hydration status, has an effect estimate of -0.17 which favors subcutaneous fluid therapy. The confidence interval is broad and includes both effect in favor of the intervention group and the control group. It is not concidered very precise on which treatment is the most effective of the two interventions. We do not have much data to conclude with from the two smallest studies (Challiner and O`Keffee), so the uncertainty around the effect estimate is considered “very serious” and two steps are downgraded in the GRADE assessment.

For outcomes, adverse effects, this is considered “not serious” on the basis of an RR of 0.74 and a confidence interval of 0.56-0.1. This favors subcutaneous fluid treatment. This result is a more precise result as the confidence interval does not include effect in favor of the control group.

5.5.5 Publication bias

It is difficult to assess publicaton bias with so few studies. To be able to test it statistically, we need at least 10 studies in the analysis (Ahmed et al., 2012). Based on this, we assess the publication bias as "Not detected".

The last 3 domain in the GRADE assessment are not relevant as we have only included RCT studies in our meta-analyzes. This applies to the following point:

- Large magnitude of an effect
- Dose –response gradient
- Effect of plausible residual confounding

The result of our GRADE judgment are shown in figur 5.

Figur 5

Summary of findings:

Subcutaneous fluid therapy compared to Intravenous fluid therapy for dehydration in the elderly above 65 y

Patient or population: dehydration in the elderly above 65 y
Setting: Nursing homes
Intervention: Subcutaneous fluid therapy
Comparison: Intravenous fluid therapy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Intravenous fluid therapy	**Risk with Subcutaneous fluid therapy**				
Hydration status (HS) assessed with: Blood sample (Serum osmoality, serum sodium follow up: mean 3 -6 days	-	SMD **0.17 SD higher** (1.34 lower to 1 higher)	-	130 (2 RCTs)	⨁◯◯◯ VERY LOW [a,b]	
Adverse effects	197 per 1 000	**146 per 1 000** (110 to 197)	**RR 0.74** (0.56 to 1.00)	832 (3 RCTs)	⨁⨁◯◯ LOW [c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **SMD:** Standardised mean difference; **RR:** Risk ratio

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

Explanations

a. Both studies was judged high risk of bias.
b. The heterogenety was 87%
c. Two studies was judge high and one was judge some conserns.

6.0 Discussion

The purpose of this study was to identify, appraise and synthesize studies examining the effect of interventons of fluid therapy in the elderly population in nursing homes, and hopefully provide with evidence to research and practice. We did this by conducting a systematic review and a meta-analysis of the data.

Results of the meta- analysis showed a small effect towards subcutanous fluid treatment compared to intravenous treatment, but the degree of confidence in the results are low. Our analysis must be interpreted in the context of the limitations of the available data.

In this discussion section, the methodological strengths and weaknesses of this systematic review will be discussed. Then, we will discuss the effect estimates of the included studies and compare its results with other research in the field and implications for further research.

6.1 Strengths and weaknesses of this systematic review

We are both nurses with expertise in elderly care. Furthermore, we are both master's students in evidence-based practice who acquire these method skills as we write this master's thesis. In addition, we have had two supervisors, one from the University College of Western Norway, and one from the National Institute of Public Health, who guided us in this method. It has given us a lot of knowledge and help along the way. We have also had a strength in working the two of us in team. Then we were able to minimize the risk of errors, at stages requires that two authors independently performes tasks in the process, for example in the process of data extraction or in rating the certainty of evidence. In addition, we have had contact with a librarian throughout the project to ensure the quality of our searches, and this has been a great strength for our master's thesis.

A strength with this systematic review is that we followed a protocol with pre-specified criterias. We published our protocol in advance, making the process transparent to the reader. Publishing a protocol also reduced duplication of effort and publication bias.

We pilot tested inclusion and exclusion criteria and the data extraction form before we started with selection, quality assessment and data extraction. Pilot testing is important to ensure a common understanding of the criteria for the work to be performed, and to be able to make necessary clarifications, adjustments and clarifications (Higgins & Thomas, 2019, p. 125). The pilot test showed that we had little need to make adjustments to the criteria for inclusion and exclusion or for the data extraction form.

We identified 3 RCT`s, which provide the highest evidence for determining intervention effect. It`s a strength that the randomisation process helps to control for unmeasured confounders that could otherwise influence the intervention effect. But we see in retrospect that there may also have been a weakness by only including this design as we did not get as many studies that met our inclusion criteria. A strong limitation of this present review are the limitations of the individual studies included in the meta-analysis. These limitations include the small sample sizes and the general lack of statistical information in two of the studies. Our analysis were therefore very limited.

In the other hand the RCT`s included are similar in population, intervention, comparison and outcome, and that gives us the opportunity to compare them.

One of our weaknesses in our methodological choices was to include only english-languaged and Scandinavian studies. Based on this, we had to exclude two studies that we could probably include in our systematic review based on the inclusion criterias. But since we did not have this linguistic competence to include them, we had no choice but to leave them out despite the fact that that choice will lead to a language bias in the overview. But overall, we are satisfied with our methodological choices for our systematic review.

We have used the validated tools, RoB 2.0 (Lefebvre et al., 2011) and GRADE (Schünemann et al., 2013) which has strengthened our systematic review.

6.1 Strength and weaknesses of the included studies

Methodological challenges and unclear reporting were a significant challenge in the included studies. Due to insufficient information in the studies and then primarily in the studies of O`Keeffe (1996) and Challiner (1994), we could not make a meta-analysis for all the data and therefore had to make a post hoc analysis for our secondary outcome measure. This was not predetermined in our protocol. The reason for that choice was that the studies did not report a mean and a standard deviation (SD), as for the outcome hydration status. The data available to us were only the number of events of the outcome and number of fluid infusions.

We had to take into account errors that could affect the results, for example if participants contributed to multiple measurements in the same analysis (unit of analysis errors). In Slesak (2003), there are more events than participants, so we can assume that this is the case. In addition, it is badly reported to the reader on how to interpret the numbers.

We also had challenges in extracting measurement data from the study of Slesak on the outcome measure, hydration status, because of the different measures on the outcome. We were in need of medical expertise from the medical profession, but we justified our choices on the basis of our nursing expertise and our textbooks on the subject. Furthermore, it was reported in Slesak that the participants were allowed to change group if there were medical- or ethical reasons for a switch between interventions. But it gave us some challenges to be able to understand who had switched interventions and at what time of the process, because of poor reporting in the studies.

It was also a methodological challenge that there were few studies included with very few participants. We were doubtful whether we would be able to make any meta-analyses based on the material we had available. And how should we interpret our results? But here the GRADE assessment was a good help in this process.

The term of external validity or generalisability describe whether or not available research evidence can be directly used to answer the research question. GRADE helped us to support our judgement about the degree of confidence in the results of the studies in our systematic review. Our two outcome measures, hydrating status and adverce effects, were judged differently.

For the outcome measure hydration status, we judged to have a very low confidence in this result. The true effect can most likely be different from what we got from our analysis, cf. section 5.5. Based on this, our findings for this outcome measure are not generalizable to the population. For outcome measures, adverse effects, we came out with a low GRADE assessment, which means that our confidence in this effect estimate is limited. And the true result will probably be different than what we got in our analysis. We can therefore not generalize this result to the population.

6.2 Comparison with existing resarch on the field and implication for further research

When we searched for knowledge on our research question, we found 6 systematic reviews that we critically evaluated after ROBIS (Whiting et al., 2016) (Appendix II). We judged the systematic review of Rochon (1997) to have a high risk of bias. They had included the same RCT study as we have, Challiner (1994) , but also the study of Dardaine (1995). We excluded Dardine because it was written in french. The conclusion in this systematic review favored subcutaneous fluid therapy as safe to administrate when electrolytes are to be given together with the fluid treatment. They found no difference in serum osmolality when comparing subcutaneous fluid therapy and intravenous fluid therapy. In additon, this study was old and we wanted to see if new studies had been added after this was made.

The systematic review of O`Keffe and Geoghegan (2000) had a narrative description where the purpose was to inform about s.c. fluid treatment. This was not relevant to answer our research question.

In 2004 the systematic review (Cassano & Turner) included four RCT studies; Challiner, Sleasak and O`Keeffe as we have done, as well as the study of Dardaine which we excluded as previously mentioned. This systematic review was also considered to have a high risk of bias. The authors of this review also considered that the evidence of effect towards subcutaneous fluid therapy was limited and that larger RCT`s studies with more validated outcome measures were needed.

The systematic review by Remington and Hultman (2007) was also assessed to have a high risk of systematic bias. Of the included RCT studies, they included the study of Slesak and O`keffe, but not Challiner (1994). But they had a restriction on their search as they only searched for English studies from 1996-2006. Their conclusion was that subcutaneous fluid therapy is as effective as intravenous fluid therapy. Nor the systematic review (Duems-Noriega & Ariño-Blasco, 1995) has been methodically gooenough to conclude with an effect on the topic. In 2016, there was once again a systematic review of the topic (Caccialanza et al.), but it was less relevant to our research question as their purpose was to provide an overview of the technique behind subcutaneous fluid therapy. Their population was unclear and it was unclear whether they had a comparison with intravenous fluid therapy.

Based on this, there was still a need to conduct our systematic review in the hope of finding more recent RCT studies that could provide us with answers to our question. We have not been able to do that, but we have identified a protocol for a new RCT study from Denmark (Nct, 2018) which looks at the same research question as us and which will hopefully add new knowledge to this topic. This study is from the hospital settings, while our purpose was to look at the same population in nursing homes. We have been in contact with them by email in the hope that we could include their study in our systematic overview, but they were unable to get their published early enough for us to include it. We will still need more RCT studies, as one study alone probably would not be enough to change practice.

7.0 Conclusion

The result of this review is to weak in order to inform practice, but it doesn´t mean that the effect of the intervention isn´t present, it only means that research havent been able to prove it yet. The methodological quality of the trials on this topic is of low and very low quality and it is does not show any effect of the intervention. Based on this we can not recommend to transfer this knowledge in to the long time care facilities. Future directions for research should include more qualitative research, and preferably RCT`s, to give high quality research on the topic.

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Appendix I A protocol for a systematic review in norwegian;

Tittel

Hvilken effekt har subkutan væskebehandling på dehydrering hos eldre i sykehjem, sammenliknet med intravenøs væskebehandling? En protokoll for en systematisk oversikt

Bakgrunn

Dehydrering hos eldre i sykehjem er en vanlig problemstilling som helsepersonell daglig må forholde seg til (Paulis et al., 2018). Eldre er på grunn av en rekke fysiologiske forandringer utsatt for et slikt overdrevent tap av kroppsvæske med eller uten salttap (Thomas et al., 2008; WHO, 2011).

Normalt sikrer homeostasen en stabil og konstant hydrering av kroppen vår (Schols et al., 2009). Denne naturlige reguleringen svikter når man blir eldre (Buffa et al., 2011; Soiza et al., 2008). Eldre får ofte en redusert tørsteføIelse som kan resultere i mindre inntak av væske og dårlig nyrefunksjon (Buffa et al., 2011; Soiza et al., 2008). Andre medisinske faktorer som for eksempel infeksjoner og medisiner kan også være med å påvirke væsketapet (Bennett et al., 2004; Schols et al., 2009). Sykehjemsbeboere har en spesiell risiko for å utvikle dehydrering da de ofte har flere faktorer som spiller inn samtidig (Gaugler et al., 2007; Wu et al., 2011). Akutt dehydrering er et resultat av et for høyt vann og natriumtap på grunn av en akutt sykdom (for eksempel infeksjon), mens kronisk dehydrering representerer en pågående væskeubalanse, vanligvis forårsaket av utilstrekkelig væskeinntak over tid (Bennett et al., 2004; Hickson & Smith, 2018). Dehydrering kan føre til forskjellige negative konsekvenser som delirium, fall, forstoppelse, urinveisinfeksjoner, nedsatt nyrefunksjon og alvorlig hypovolemi som fører til lavt blodtrykk med organsvikt som følge (Hooper et al., 2014). Dette kan være med å påvirke den eldre sin livskvalitet og øke risikoen for dødelighet betydelig (Courtney et al., 2009).

En systematisk oversikt (Paulis et al., 2018) viste en forekomst mellom 0,8-38,5% av de eldre som var dehydrerte i sykehjem. Bakgrunn til den store variasjonsbredden i forekomsten ligger i at de 19 inkluderte studiene i oversikten brukte ulike metoder for å måle dehydrering på, samt at det ikke kom tydelig frem hvilken type dehydrering som ble målt (kronisk eller akutt). Oversikten avdekket også 49 risikofaktorer for at eldre i sykehjem ble dehydrert. Kognitiv svekkelse og feber var blant de høyeste. Et av behandlingsalternativene til dehydrering er intravenøs væskebehandling, en behandlingsform som krever sykepleierkompetanse. Denne kompetansen består blant annet i at sykepleier må legge inn en

perifer venekanyle i pasientens blodåre og væsken blir deretter transfundert inn i blodbanen til pasienten. Denne væskebehandlingen må følges tett opp av sykepleier. Dersom sykehjemmet mangler denne kompetansen må pasientene i disse tilfellene innlegges i sykehus. Det er verken bra samfunnsøkonomisk eller gunstig for pasienten. En systematisk oversikt (Pershad, 2010) som viser sykehuskostnadene ved væskebehandling, antydet at kostnadene ville være lavere med oral og subkutan rehydrering, enn med intravenøs væskebehandling. Oral rehydrering vil alltid være å foretrekke i disse situasjonene, men det er ikke alltid at pasienten tar til seg nok væske via munnen. Den planlagte systematiske oversikten, skal derfor se på effekten av subkutan væskebehandling som en alternativ måte å rehydrere disse pasientene på, som vil kreve mindre sykepleieressurser. Ved subkutan væskebehandling gies som oftes natriumklorid 0,9% via en liten kanyle som typisk blir injisert i underhudsfettet på låret, magen eller overarmene. Væsken blir så transportert bort fra underhudsfettet og inn i cellene ved hjelp av diffusjon (Osmose) (Henriksson et al., 2014, pp. 16-17). Man kan gi inntil 3000 ml /24 timer væske subkutant ved mild til moderat dehydrering (Walsh, 2005, p. 124). Ved alvorlig dehydrering kan det være påkrevd med intravenøs væskebehandling. Det kan da være klinisk indikasjon på å gi større mengder væske som kan transfundere inn på kortere tid for å opprettholde et optimalt blodtrykk (Agrò, 2013, p. 143). Subkutan væskebehandling kan også være aktuelt i de tilfeller hvor man ikke klarer å legge inn en perifer venekanyle som for eksempel hos eldre som har skjøre årer som sprekker lett (Walsh, 2005, p. 124).

Det finnes i dag forskningsoversikter over denne problemstillingen, men de jeg har funnet vurderes til å ha høy risiko for systematiske skjevheter (se kritisk vurdering av de 6 relevante oversiktene utført med ROBIS verktøyet i vedlegg 2) og det kan påvirke resultatet. Det blir derfor vanskelig å stole på disse resultatene som fremgår i oversiktene. I tillegg var noen av oversiktene av gammel dato og nyere studier kan ha tilkommet som kan sammenfattes i ny oversikt som kanskje gi noen mer validerte svar på dette forskningsspørsmålet.

Søket jeg utførte var i Cohrane Library, Medline, Embase og PROSPERO (se vedlegg 1, søkeord og søkestrategi).

I PROSPERO finnes en protokoll for en systematisk oversikt, fra Brasil (Andrade et al., 2017), en tilsvarende protokoll for et SR, som jeg planlegger å gjøre, men den er kraftig forsinket og det er usikkert hvorvidt den fremdeles jobbes med. Det har blitt gjort forsøk på å kontakte dem pr mail, uten respons. Senterleder for kunnskapsbasertpraksis ved høyskolen på Vestlandet, Birgitte Graverholt, har også gjort forsøk på å kontakte forskerne til denne protokollen uten hell. (se vedlegg nr 3,4,5 og 6)

Man velger derfor å gå videre med dette prosjekt da kunnskapen som dette SR prøver å finne svar på, vil bli et viktig bidrag i fremtidig praksis ved dehydrering hos eldre i sykehjem.

Formål

Formålet med denne systematiske oversikten er å undersøke om subkutan væskebehandling kan være en optimal behandlingsform for dehydrerte pasienter i sykehjem og da være med å bidra til oppsummert kunnskap på dette temaet.

Forskningsspørsmål

" Hvilken effekt har subkutan væskebehandling sammenliknet med intravenøs væskebehandling, på dehydrering hos eldre i sykehjem?"

Metode

Det planlegges for en protokoll for et effektspørsmål. Et SR kjennetegnes ved at det er systematisk gjennomført og transparent for leser (Hoffmann, 2017, p. 295). Kriteriene for å skrive et SR om effekt av tiltak, er godt beskrevet i Cochrane handbook for systematic reviews of interventions (Higgins & Thomas, 2019) og i PRISMA-P (Shamseer et al., 2015). Jeg kommer derfor til å referere til de begge når jeg nå fordyper meg i denne metoden for min protokoll til den systematisk oversikten.

Inklusjons- og eksklusjonskriterier:

I PICO spesifiserer jeg inklusjons og eksklusjonskriteriene som anbefalt i PRISMA-P (Shamseer et al., 2015, p. 7)

Populasjon/ deltakere:

Jeg inkludere studier som har undersøkt eldre fra 65 år og oppover.

Intervensjon og sammenlikning:

Studier som sammenlikner subkutan væskebehandling med intravenøs væskebehandling, til behandling av mild til moderat dehydrering hos beboere/pasienter i sykehjem, vil bli inkludert i oversikten. Dersom det finnes få studier av dette fra sykehjem vil jeg inkludere studier fra sykehus. Dette vil bli vurdert underveis i prosessen. Det settes ingen restriksjoner på væsketype, dosering eller varighet av væskebehandlingen.

Utfallsmål

Primærutfallsmål er hydreringsstatus målt ved osmolalitet, urea eller mean arterial pressure (MAP), men ekskludere ikke studier som har målt hydreringsstatus på andre måter.

Sekundærutfallsmål er å se på komplikasjoner ved disse to administrerings metodene av væskebehandlingen. (subkutan eller intravenøs metode)

Studiedesign:

Systematiske oversikter (SR) med lav risiko for skjevhet som kun har inkludert randomiserte kontrollerte studier (RCT) som er gullstandarden for å avdekke effekt av tiltak (Polit & Beck, 2012, p. 28). Dersom jeg ikke finner SR av med lav risiko for skjevhet inkluderes RCT.
Ved randomiserte kontrollerte studier blir deltakerne tilfeldig fordelt (randomisert) til enten intervensjonsgruppen eller kontrollgruppen, slik at man skal kunne se om effekten kan tilskrives tiltaket og ikke (Hoffmann, 2017).

Litteratursøk

Jeg ønsker å identifisere så mange RCT studier og kvantitative systematiske oversikter som mulig, og setter opp en bred søkestrategi som kan gi mange relevante treff, med minst mulig begrensninger på. Cochrane handbook (Higgins & Thomas, 2019), anbefaler at man inkluderer studier fra alle språk, men i min oversikt må jeg dessverre begrense meg til engelsk språklige, eller skandinaviske studier, for å kunne vurdere dem. Jeg har utformet en foreløpig søkestrategi (se vedlegg nr 1) for å undersøke hva som allerede fantes av tidligere forskning på området. Denne strategien tar jeg med meg i møte med en bibliotekar for å prøve å utvide og forbedre strategien ytterligere, slik at jeg kan fange opp mer og forhåpentligvis nyere studier på mitt forskningsspørsmål. Databasene jeg til nå har søkt i er, Cochrane Library, EMBASE og MEDLINE. De samme databasene kommer til å bli benyttet i videre søk, da dette er i tråd med anbefalingene fra Cochrane (Higgins & Thomas, 2019 Kap 4.3). I tillegg anbefales det å gjøre søk i den fagspesifikke databasen CINAHL (Lund et al., 2014, p. 49). Det vil også bli søkt i Epistemonikos etter relevante systematiske oversikter.
Jeg planlegger å søke etter relevante RCT studier samt relevante systematiske oversikter, sistnevnte for å kunne gjennomgå referanselistene, og prøve å oppdage nye studier, som ikke er blitt fanget opp i søkene mine. Jeg kommer også til å utføre siteringssøk i Web of sience og søke etter grå litteratur i Open Grey. Søket mitt vil også vil bli kvalitet sikret ved at

bibliotekar benytter den kunnskapsbaserte sjekklisten fra PRESS (Peer Review of Electronic Search Strategies) (McGowan et al., 2016).

Utvelgelse av studier:

Studiene jeg finner i søkene, vil først bli screenet for dublikater i endnote og deretter overført til programmet Covidence (*Covidence*, 2019). Derfra vil de bli vurdert av to personer uavhengig av hverandre i alle fasene av utvelgelsen (Moher D, 2015, p. 11). I den første screeningen går man gjennom studiene og ser på tittel og abstrakt. Studiene sorteres i tre klassifiseringer; relevant, usikker og eksludert. I fase to sjekkes de igjen av begge personene (uavhengig av hverandre) om studiene møter inklusjons og ekslusjonskriteriene. For å forsikre seg om at man er enig i første fase, så sitter man sammen når man gjennomgår de 10 første studiene. Uenigheter vil bli løst ved diskusjon eller ved å ta inn en tredjepart hvis man ikke blir enig. Relevante og usikre studier, vil bli innhentet i fulltekst og gjennomgått (av to uavhengige personer) nok en gang for å sørge for at bare relevante studier blir inkludert i oversikten. Studier som ikke er på engelsk, norsk, dansk eller svensk, vil bli ekskludert, da det ikke vil være mulig å få vurdert dem. Hele denne utvelgelsesprosessen vil bli vist i et flytdiagram (Moher D, 2015).

Uthenting av data fra studier

Dataene vil bli uthentet av to uavhengige personer ved å bruke et datauthentingskjema, som vil bli laget på forhånd (Moher D, 2015, p. 11). Hvis det oppstår uenigheter, vil dette blir løst ved diskusjon med hverandre og ved å ta inn veileder, som en tredje person i saken, dersom man ikke blir enig. Dataene som hentes ut vil bli presentert i en tabell. Data som blir aktuell å hente ut er; Studieland, antall deltakerer i intervensjon - og kontrollgruppen, frafall, studietid, utfallsmål og alder, kjønn, effektmål, effektestimat. Intervensjonsgruppen er de som mottar subkutan væskebehandling uavhengig av væskemengde, væsketype og behandlingstid og kontrollgruppen er de som får intravenøs væskebehandling, uavhengig av væsketype, mengde og behandlingstid.

Videre uthentes data på hydreringsstatus målt i osmolalitet, urea eller mean arterial pressure (MAP) og eventuelt andre måter å måle dette på. Samt om det er blitt målt albuminstatus på deltakerne før behandlingen startet. Det vil også bli hentet ut data som omhandler rapporterte komplikasjoner som for eksempel sår ved det subkutane innstikkstedet, smerter som følge av økt væske ved innstikkstedet og tromboflebitt ved det intravenøse innstikkstedet,etc.

Datauthentingskjemaet vil bli pilotert (testet ut) av to ulike personer. Dette er med på å sikre datauthentingen (Moher D, 2015, p. 11).

Vurdering av risiko for systematiske feil i studiene.
Risiko for systematiske skjevheter i SR vil bli vurdert med norsk versjonen av verktøyet ROBIS: "Tool to asess risk of bias in systematic reviews" (Whiting et al., 2016) (se vedlegg 7).
Fase 1 av ROBIS vurderer oversikten for *relevans* i forhold til egen pico.
Fase 2 består av 4 ulike domener i forhold til metodisk fremgangsmåte:
Domene 1 omhandler spørsmål knyttet til kriterier for utvelgelse av studier.
Domene 2 går på identifikasjon og utvelgelse av studier.
Domene 3 handler om dataekstraksjon og vurdering av studier
Domene 4 ser på syntesen og funn
Hvert domene sammenfatter innvendingene i "*få, mange eller uklare*" i forhold til metode.
Og til slutt i Fase 3 vil helheten bli vurdert og oppsummert og endelig risikoen for systematiske skjevheter i oversikten vil bli vurdert som enten lav, høy eller uklar.

Risiko for skjevhet i RCT vil bli vurdert ved bruk av RoB2 (Risk of Bias) som er det anbefalte verktøyet fra Cochrane (Higgins & Thomas, 2019, p. Kap 8). I ROB2 gjennomgås fem domener for deretter å komme ut med en oppsummert risiko for skjevhet i studien. Studien kan få tre forskjellige utfall etter den kritiske gjennomgangen; lav risiko for skjevhet, noen bekymringer i studien som kan ha påvirket resultatet eller en høy risiko for skjevhet i studien.
De fem domenene som gjennomgås i den kritiske vurderingen er (Sterne et al., 2019):

1) Seleksjonsskjevhet (Allocation/selection bias)
2) Utøverskjevhet (Performance bias)
3) Måleskjevhet (Measurement bias)
4) Frafallskjevhet (Attrition bias)
5) Publiseringsskjevhet (Publication bias)

Studier med lavere risiko for systematiske skjevheter vil bli lagt større vekt i den systematiske oversikten. Studier får lav risiko for bias dersom alle domenene er blitt metodisk korrekt gjennomført.

To uavhengige personer vil gjøre disse vurderingene i ROBIS og RoB2.
Uenigheter løses med konsensus. En tredje person vil også her taes inn hvis man ikke er blir enig. Jeg vil presentere alle studiene i en figur som skal vise en oppsummering av risikoen for bias i de inkluderte studiene i oversikten.

Analyse og datasyntese

Dersom studiene er like nok vil de bli presentert i en metaanalyse, hvor alle dataene med de samme utfallsmålene blir satt sammen og presentert i egne "forest plot" (Lund et al., 2014, pp. 148-149). Da vil jeg komme til å få flere synteser med ulike utfallsmål presentert. Like data på væskemengde, væsketype og behandlingstid vil bli satt sammen i egne synteser. Og like data på de ulike komplikasjonene vil bli satt sammen i analysen.

Jeg vil benytte programvaren "Revman" (*Revman 5*, 2019) til å lage denne metaanalysen. Videre skal jeg sammenfatte studier med samme populasjon, da vil det være mest hensiktsmessig å bruke en fixed effekt model, i motsetning til en random effekt model, hvor man antar at det er en viss variasjon mellom studiene (Lund et al., 2014, p. 151). Men dette må vurderes ytterligere når man har ser hvilke studier som har blitt inkludert i syntesen.

Hvilken type data som blir presentert i de ulike inkluderte studiene, vil være med på å bestemme hvilke typer analyse som kan gjøres. For dikotome data brukes relativ risiko og for kontinuerlige data brukes gjennomsnittsforskjeller (MD) eller SMD (standadiserte gjennomsnittsforskjeller). For begge typer utfallsmål vil jeg oppgi et 95% konfidensintervall og en p-verdi, hvis mulig. I metaanalysen planlegges det å vise en Tau^2 for å få et mål på hvor stor variasjon det er mellom de observerte effektene studienene. For å vite om disse funnene er en tilfeldighet eller ikke måles også en Chi^2 test. Det er også ønskelig med en I^2, heterogenitetstest, for å vise hvor stor andel av variasjonen som ikke kan forklares av tilfeldigheter. En heterogenitet fra 0-40% betyr lite for resultatet da det er ønskelig med en viss variasjon mellom studiene som inkluderes, på bakgrunn av den eksterne validiteten. 30-60% er en moderat forskjell mellom studiene. Fra 50% og oppover er det en betydelig forskjell som da vil påvirke troverdigheten av resultatet i oversikten (Lund et al., 2014, p. 151). I slike tilfeller med en høy I^2 vil det blir laget en subgruppeanalyse og en sensitivitetsanalyse for å se etter feil i analysen.

Dersom studiene er for ulike til at resultatene kan sammenfattes i metaanalysen, vil de bli presentert i en "beskrivende" syntese (Petticrew & Roberts, 2006, p. 164). En slik subjektiv metode kan frembringe systematiske skjevheter dersom noen studieresultater blir vektlagt mer enn andre. Jeg kommer derfor til å vektlegge en transparent fremstilling for hvordan dette er blitt gjort.

Det vil også bli laget en tabell for å oppsummere resultatene fra de ulike studiene. I denne oversikten vil jeg presentere de ulike studiene, resultatene på effekt av intervensjons og kontrollgruppen og oversikt over hvilke risikoer for skjevhet de ulike studiene har.

Vurdering av kvaliteten på dokumentasjonen

Videre vil jeg benytte GRADE (Guyatt et al., 2011) og programvaren GRADE-pro (*GRADEpro*, 2020) for å foreta en samlet vurdering av kvaliteten på de inkluderte studiene i oversikten. To forfattere vil utføre denne vurderingen. Ved uenighet vil en tredje person bli rådført.

Domenene i GRADE er:

1) Studiebegrensninger
2) Direkthet
3) Konsistens
4) Presisjon
5) Rapporteringsskjevhet
6) Sterke sammenhenger mellom tiltak og utfall
7) Dose – responseffekter
8) Forvekslingsfaktorer

Kvalitetensvurderingen i GRADE kan gi en av fire ulike vurderinger:

1) Høy kvalitet betyr at man har stor tillitt til at effektestimatet ligger nær den sanne effekten
2) Middels kvalitet vil si at effektestimatet ligger sannsynligvis nær den sanne effekten, men at det også kan være en mulighet for at den kan være forskjellig
3) Lav kvalitet betyr at vi har en begrenset tillit til effektestimatet. Den sanne effekten kan være vesentlig ulik effektestimatet.
4) Svært lav kvalitet vil si at vi har svært liten tillitt til at effektestimatet ligger nær den sanne effekten.

Begrensinger ved valgt tilnærming

Ved å bare søke etter RCT studier som har sammenliknet subkutan væskebehandling med intravenøs væskebehandling, kan jeg risikere å få for lite studier å inkludere i oversikten. Dette er også bakgrunn til at jeg også velger å søke etter studier gjort på sykehus på eldre for da overføringsverdien her til sykehjem er stor. Jeg kan også gå glipp av relevante studier hvor språket ikke er forståelig, da jeg bare velger å inkludere skandinavisk og engelsk språk. Men jeg er åpen for å søke i flere databaser hvis bibliotekar mener at det er hensiktsmessig.

Etiske vurderinger

Ingen av de personene som skal arbeide med denne systematiske oversikten har noen interessekonflikter eller mottar noen form for økonomisk støtte som kan påvirke resultatet i oversikten. Kun studier som har fått etisk godkjenning vil bli inkludert i oversikten.

Formidling

Jeg vil undersøke mulighetene for å publisere min systematiske oversikt i bladet" Sykepleien forskning", slik at det når ut til sykepleiere som jobber med denne utfordringen til dagen. Videre ønsker jeg å formidle kunnskapen til avdelingsledere, enhetsledere og etatsdirektør i etat for sykehjem i Bergen kommune. Formidlingen kan skjer i ulike lederfora jeg sitter i som avdelingsleder, og stedfortreder for styrer ved en sykehjemsenhet. Samt formidle kunnskapen til fagkonsulentene i etat for sykehjem i Bergen via enhetslederne.

Fremdriftsplan

	Aug/ Nov 19	**Jan/ Feb 20**	**Mars/ April20**	**Mai/ Juni20**	**Juli/ Aug20**	**Sept/ Okt 20**	**Nov/ Des 20**	**Jan/ Feb 21**	**Mars - Mai 21**
Prosjektbeskrivelse									
Søkestrategi									
Litteratursøk									
PRESS									
Utvelgelse av studier									

Pilotere datainnsamling										
Pilotere kvalitetsvurdering										
Datauthenting										
Vurdering av risiko for systematiske skjevheter										
Data analyse										
Skrive innlednings-del (Kappe)										
Skrive artikkel										

Referanseliste til protokoll

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Appendix II Attatchment to the protocoll in norwegian

Attatchment 1 of 2

Preliminary keywords and search strategy:

	P: Dehydrering hos eldre over 65 år i sykehjem	I: Subcutan væskebehandling
Emneord i Cochrane Library	Dehydration	Fluid Therapy Hypodermoclysis Infusions, Subcutaneous Infusions, Parenteral Infusions, intravenous Administration, intravenous
Emneord i MEDLINE	Dehydration	Fluid Therapy Rehydration solutions Infusions, intravenous Infusions, parenteral
Emneord i EMBASE	Dehydration	Fluid Therapy
Tekstord:	Dehydration Dehydrated Water Stress Stress, Water	Fluid therapy Therapy, Fluid Fluid Therapies Therapies, Fluid Rehydration Rehydrations Infusions, intravenous Infusions, parenteral Infusions, subcutaneous Hypodermoclyses Hypodermoclysis Administration, intravenous Administration, subcutaneous Fluid

Ikke relevante ord:	• Hypercalcemia ▪ Hyperkalemia ▪ Hypernatremia ▪ Hypocalcemia ▪ Hypokalemia ▪ Hyponatremia Wather intoxication	Oral Rehydration Therapy Therapy, Oral Rehydration Rehydration Therapy, Oral Oral Rehydration Therapies Rehydration Therapies, Oral Therapies, Oral Rehydration Oral Rehydration Oral Rehydrations Rehydrations, Oral Rehydration, Oral

MEDLINE

1 dehydration/ (37713)

2 dehydrat*.tw. (49226)

3 water stress.tw. (3309)

4 1 or 2 or 3 (70649)

5 fluid therapy/ (20481)

6 fluid therap*.tw. (4263)

7 Rehydration*.tw. (8746)

8 hypodermoclysis.tw. (139)

9 5 or 6 or 7 or 8 (29699)

10 4 and 9 (5325)

11 limit 10 to "therapy (best balance of sensitivity and specificity)" (593)

12 from 11 keep 27,36,75,120,216,220,357,370,375,399,457-458,529 (13)

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Gjennom gikk 13 relevante artikler.

Funn i PROSPERO**:**

Nct. (2018). Subcutaneous vs Intravenous Hydration on Older Adults. *Https://clinicaltrials.gov/show/nct03710408*. Hentet fra https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01664216/full

Denne protokollen er fra Brasil og studien skulle være ferdig i februar 2018, men jeg kan ikke finne det ferdige produktet. Jeg har sendt en mail til prosjektleder uten å få svar ang status på denne protokollen. Etter veiledning fra lærer, kan man tillate seg å gå videre med mitt prosjekt da denne er kraftig forsinket.

I tillegg har jeg gjennomgått referanselister til aktuelle artikler jeg fant i søkene.

Vedlegg til protokoll nr 2

Prosjektplan

Litteraturtabell over 6 relevante oversiktsartikler som jeg fant etter søkene.

"Et SR (systematisk oversikt) er bare så god som de studiene de baserer seg på" (Hans Lund)

Oversikt nr: 1	**Populasjon**	**Intervensjon**	**Sammen likning**	**Utfallsmål**	**Formål**
Hypo-dermoclysis to treat dehydration: A review of the evidence. (Remington & Hultman, 2007) USA	**Eldre 71-85 år**	S.c. væske behandling ved dehydrering	Intravenøs væske behandling ved dehydrering	Rehydrering: Måler på serum urea og kreatinin og serum sodium	**Primærmål:** Vurdere sikkerhet og effekt av subkutan væskebehandling til behandling av mild til moderat dehydrering. **Sekundærmål:** Å sammenlikne s.c. og iv. væskebehandling .
Konklusjon	Subkutan væskebehandling er like effektiv som intravenøs væskebehandling.				
Kritisk vurdering etter ROBIS (Whiting et al., 2016) Fase 1-3 Domene 1-4.	**Fase 1:** Den systematiske oversikten er relevant for min PICO. **Fase 2** **Domene 1**: Mangelfull beskrevet metode del. Lite gjennomsiktig for leser. Beskriver ingen protokoll. Utvelgeskriteriene: Engelske studier fra 1996-2006. Ekskluderte studier som omhandlet subkutan administrasjon av medikamenter eller hvor de gav subkutan væske for andre tilstander enn dehydrering eller hvor det omhandlet alvorlig dehydrering. 8 studier ble inkludert, 2 RCT og 6 kohortstudier. 4 fra sykehjem, 2 fra geriatrisk sykehus, 1 hospice og 1 fra sykehus. Studiekvaliteten på de inkluderte studiene var lav. Utvalget på noen av studiene var lite, og de fleste studiene var ikke blindet. I en RCT fikk 19 deltakere lov til å skifte hvilken gruppe de tilhørte, basert på kliniske vurderinger, og dette skjedde oftere enn forventet. Bare tre av studiene sammenliknet effekten. Nr 16,18 og 19 i referanselisten. 2 RCT og 1 prospektiv observasjonsstudie. **Domene 2:** Søkt i Medline, cochrane Library, Embase, CINAHL, og Joanna Briggs Institute. Hensiktsmessige databaser. Søkestrategi mangler. Kun søkt på MeSH ordene: Hypodermoclysis, clysis, fluid therapy, subcutaneous, dehydration og hydration. Ikke tekstordsøk. Fikk treff på 29 aktuelle studier. Beskriver ikke at utvelgelsen av studiene ble gjort av to uavhengige personer. Her er stor risiko feil. **Domene 3:**Metodene for dataekstrasjon og vurdering av studiene er ikke beskrevet. Det er ikke skrevet om bias i de inkluderte studiene. **Domene 4:** Metodene som ble brukt for å sammenfatte studiene er ikke beskrevet. Alle de 8 inkluderte studiene ble presentert i en tabell. Det er ikke beskrevet noe om forhåndsdefinerte analyser. Ikke gjennomført en analyse. **Fase 3:**				

	Denne oversikten vurderes til å ha høy risiko for systematiske skjevheter. Basert på denne systematiske oversikten trengs det en ny og oppdateret kunnskap på dette temaet. Studien er 12 år gammel og nyere studier kan ha tilkommet.
RCT studier i oversikten	• Comparison of subcutaneous and intravenous rehydration in geriatric patients (G. Slesak et al., 2003) • Subcutaneous fluids in elderly hospital patients with cognitive impairment (O'keeffe & Lavan, 1996)

Oversikt nr: 2	**Populasjon**	**Intervensjon**	**Sammen likning**	**Utfallsmål**	**Formål**
A systematic review of the evidence for hypo-dermoclysis to treat dehydration in older people (Rochon et al., 1997)	Eldre i sykehjem	S.c. væske behandling ved dehydrering	18 inluderte studier, bare 2 RCT som sammen liknet effekten mellom i.v og s.c væskebehandling.)	Rehydrering. Serum osmolalitet ble målt.	Formålet med denne oversikten var å finne bevis som støttet bruk av subkutan væskebehandling og drøfte bruken av dette i klinikken i sykehjem
Konklusjon	Subkutan væskebehandling kan bli brukt og er en sikker administrasjonsform når man skal gi elektrolytter i sammen med væskebehandlingen. " Ingen forskjell i serum osmolalitet når man sammenliknet subkutan og intravenøs væsketilførsel"				
Kritisk vurdering etter ROBIS (Whiting et al., 2016) Fase 1-3 Domene 1-4.	**Fase 1:** Den systematiske oversikten er delvis relevant for min PICO. Liten sammenlikning med intravenøs væskebehandling. **<u>Fase 2</u>** **Domene 1**: Mangelfull beskrevet metode del. Lite gjennomsiktig for leser. Beskriver ingen protokoll. Utvelgeskriteriene: Engelske studier som omhandlet subkutan væskebehandling . Av 18 inkluderte studier var det bare 2 RCT som sammenliknet effekten mellom intravenøs og subutan væskebehandling. **Domene 2:** Søkte kun i Medline. Søkestrategi mangler. Søkte på tekstordet " hypodermoclysis" og MeSH ordene: "fluid therapy, hyaluranidase, subcutaneous injections, parenteral infusions, parenteral nutrition" Dette gav et treff på 5619 artikler, de begrenset på alder og endte med 432 artikler. Etter å ha lest tittel og abstrakt endte de ned i 18 relevante studier som de inkluderte i oversikten. Søkene de har utført her er lite systematiske og de har ikke gjort søk i andre relevante databaser. Men de har forsøkt å finne flere studier fra referanselister. Beskriver ikke at utvelgelsen av studiene ble gjort av to uavhengige personer. Her er stor risiko feil. **Domene 3:**Metodene for dataekstrasjon og vurdering av studiene er ikke beskrevet. Det er ikke skrevet om bias i de inkluderte studiene eller om hvilke studiedesign de ulike studiene er. **Domene 4:** Metodene som ble brukt for å sammenfatte studiene er ikke beskrevet. Alle de 18 inkluderte studiene ble presentert i en tabell. Det er ikke beskrevet noe om forhåndsdefinerte analyser. Det er ikke gjennomført en analyse av funnene. **Fase 3:** Denne oversikten vurderes til å ha høy risiko for systematiske skjevheter. Forfatterne skriver selv at størsteparten av de inkluderte studiene var av svært dårlig kvalitet og at man trenger derfor nye studier med god kvalitet for å kunne vurdere behandlingseffekten av s.c væskebehandling. I tillegg er denne oversikten gammel og utdatert. Denne studien er veldig gammel og nyere studier kan ha tilkommet.				
RCT studier i review	• A comparison of intravenous and subcutaneous hydration in elderly acute stroke patients (Challiner et al., 1994) • Metabolic and hormonal changes induced by hypodermoclysis of glucose – sailine solution in elderly patients. (Dardaine et al., 1995)				

Oversikt nr: 3	Populasjon	Intervensjon	Sammenlikning	Utfallsmål	Formål
Subcutaneous dextrose for rehydration of elderly patients – an evidence-based review (Cassano & Turner, 2004) London	**Eldre pasienter** **4 inkluderte studier.** **1 SR** (Rochon et al., 1997) **2 RCT** **1 Cohort**	Subcutan væske-behandling tilført 5% dextrose	Intravenøs væske behandling tilført 5% dextrose	Rehydrering	Å vurdere sikkerhet og finne ut av hvilke behandling som er best for pasienten av intervensjonen eller sammenlikningen?
Konklusjon	Subkutan væsketilførsel med dextrose kan bli brukt effektivt i pasientbehandling av dehydrering til eldre. Men bevisene er begrenset og større RCT studier med validerte utfalsmål er nødvendig for å bekrefte disse funnene.				
Kritisk vurdering etter ROBIS (Whiting et al., 2016) Fase 1-3 Domene 1-4.	**Fase 1:** Den systematiske oversikten er relevant for min PICO, selv om jeg ikke ser på væske tilført dextrose. Det kan ha en overføringsverdi. **<u>Fase 2</u>** **Domene 1**: Beskriver ingen protokoll. Utvelgeskriteriene:. Engelske studier fra 1993-2003. **Domene 2:** Søkt i Cohrane Library, Medline, IDIS, CINAHL, Current Contents, Premedline, Australasian Medical Index, The Joanna Briggs Institute, the US National Guideline. Søkene var utført i 2003 og er nå 16 år gamle. Nyere studier kan ha tilkommet. Det er ikke gjort søk i Embase og de kan derfor ha "mistet" noen relevante treff. Forfatterne beskriver søkestrategi med at de kombinerte søketermer som: hypodermoclysis, clysis, fluid therapy, infusion, subcutaneous injection, og kombinerte dem med dextrose, glucose også begrenset de til eldre pasienter uten å oppgi noen alder på det. Beskriver ikke MeSH termer men det fremgår av vedlagt søkestrategi for Medline. Denne ser hensiktsmessig ut, men kan med fordel utvides. **Domene 3:**Dataekstraksjonen er lite beskrevet, men ble kun utført av 1 person og vurdering av studiene er ikke beskrevet. De skriver at oversikten (Rochon et al., 1997) hadde mange begrensinger som dårlig søkestrategi, minimal vurdering av validitet av de inkluderte studiene, liten analyse av funnene og ingen statistisk metaanalyse var tatt. Studiene var bare gruppert og diskutert etter studiedesign. I slesak at al. var det stort frafall fra gruppen som fikk subkutan væske for så å gå over i kontrollgruppen. **Domene 4:** Metodene som ble brukt for å sammenfatte studiene er ikke beskrevet. Alle de 4 inkluderte studiene ble presentert i en tabell. Det er ikke beskrevet noe om forhåndsdefinerte analyser. Analysen var ikke hensiktsmessig. De systematiske feilene i studiene var ikke tatt hensyn til i analysen. Funnene presenteres i en tabell hvor det kritisk kommenteres hver enkelt studie. **Fase 3:** Denne oversikten vurderes til å ha høy risiko for systematiske skjevheter. Basert på denne systematiske oversikten trengs det en ny og oppdateret kunnskap på dette temaet. Forfatterne beskriver selv at bevisene på området er begrenset og studiene som er blitt vurdert har metodiske feil som gjør at styrken på bevisene blir svak. Man trenger RCT studier som er metodisk god og som bruker validerte utfallsmål for å kunne bekrefte disse funnene i vår oversikt.				
RCT studier i oversikten	• A comparison of intravenous and subcutaneous hydration in elderly acute stroke patients (Challiner et al., 1994) • Metabolic and hormonal changes induced by hypodermoclysis of glucose – sailine solution in elderly patients. (Dardaine et al., 1995) • Subcutaneous fluids in elderly hospital patients with cognitive impairment (O'keeffe & Lavan, 1996) • Comparison of subcutaneous and intravenous rehydration in geriatric patients: a randomized trial. (Günther Slesak et al., 2003)				

Oversikt nr: 4	Populasjon	Intervensjon	Sammen likning	Utfallsmål	Formål
Subcutaneous hydration in the elderly. Review (O'Keeffe & Geoghegan, 2000)	Eldre i sykehus? Uklart	Subkutan væske behandling	Intravenøs væske behandling	Ingen	Forfatter har ikke definert formål med oversikten, men leser antar at det er ment som generell informasjon om subkutan væskebehandling.
Konklusjon	Subkutan væskebehandling er trygt og effektiv behandling for å forebygge mild dehydrering til pasienter som ikke tar til seg tilstrekkelig væske per oralt. Sammenliknet med intravenøs væskebehandling er subkutan væskebehandling spesielt god til pasienter som har dårlige årer å stikke i og til de med kognitiv svekkelse samt til pasienter som holder på med aktiv rehabilitering.				
Kritisk vurdering etter ROBIS (Whiting et al., 2016) Fase 1-3 Domene 1-4.	Denne oversikten er ikke gjennomført systematisk. Ikke gjennomsiktlig for leser. Forfatter beskriver ikke formål med oversikten. Den er narrativ. Har ingen metodebeskrivelse og tilsynelatende ingen protokoll. Ingen søkebeskrivelse, ingen inklusjons eller eksklusjonskriterier. Den narrative teksten, refererer til enkeltstudier gjennom hele oversikten. Det kommer ikke klart frem hvilket studiedesign disse studiene er. Det er ikke satt opp noen analyse av funn i denne oversikten. Og har ikke definert noen utfallsmål. . De inkluderte studiene blir ikke vurdert for bias. Den vurderes derfor til å ha høy risiko for systematiske skjevheter				
RCT studier i oversikten	• Uklart				

Oversikt nr: 5	Populasjon	Intervensjon	Sammen likning	Utfallsmål	Formål
Subcutaneous Infusion of fluids for hydration or nutrition: A Review 2016 (Caccialanza et al., 2016)	Alle? Barn Voksne Eldre	Subkutan væske behandling	Uklart! Noen av de inkluderte studiene sammenlikner med intravenøs væske behandling		Å skaffe en oversikt av teknikken og sammenfatte funnene fra kliniske studier, inkludert de som er relatert til sikkerhet og presentere fordelene og bakdelene ved subkutan væskebehandling og indikasjonene for dette.
Konklusjon	De tilgjengelige bevisene foreslår at subkutan væskebehandling kan være en effektiv teknikk for væskeadministrasjon ved dehydrering som har minimale komplikasjoner. Bevisene som tyder i denne retning kommer fra relativt små RCT studier eller observasjons studier. Vi trenger derfor høykvalitets RCT studier for å kunne konkludere.				
Kritisk vurdering etter ROBIS (Whiting et al., 2016) Fase 1-3 Domene 1-4.	**Fase 1:** Den systematiske oversikten er delvis relevant for min PICO men har en uklar populasjon. Formålet med oversikten er mindre relevant for mitt forskningsspørsmål. **Fase 2** **Mangelfull beskrevet metode del. Lite gjennomsiktig for leser.** **Domene 1**: Beskriver ingen protokoll. Utvelgeskriteriene er ikke beskrevet. **Domene 2:** Søkt i Medline, Embase, Biosis. Har ikke søkt i Cochrane Library som er anbefalt. Kunne også søkt i fagspesifikk database, CINAHL. Søkeord: Hypodermoclysis, clysis, og subcutaneous fluid. Det beskrives ikke hvordan søket er blitt utført og om man har brukt MeSH ord og tekstord seperat. Søkeordene er mangelfulle og man kan med fordel finne flere ord for å få bedre og flere treff. Det er 13 inkluderte studier i oversikten.9 av dem er RCT og 7 av dem omhandler eldre. Andre studier omhandler kreftpasienter og barn. Denne gruppen er lite sammenlingbar. **Domene 3:**Metodene for dataekstrasjon og vurdering av studiene er ikke beskrevet. Det er ikke skrevet om bias i de inkluderte studiene. **Domene 4:** Metodene som ble brukt for å sammenfatte studiene er ikke beskrevet. Alle de 13 inkluderte studiene ble presentert i en tabell. Det er ikke beskrevet noe om forhåndsdefinerte analyser. Analysen var ikke hensiktsmessig grunnet ulik populasjon. De systematiske feilene i studiene var ikke tatt hensyn til i analysen. **Fase 3:** Denne oversikten vurderes til å ha høy risiko for systematiske skjevheter.				

	Forfatterne av oversikten konkluderer at man trenger flere RCT studier med høy kvalitet for å kunne konkludere med en sikker effekt av subcutan væskebehandling.
RCT studier i oversikten	6 som omhandler eldre. (Oppgitt 7 RCT, men den ene var prospektiv) Hypermoclysis in dehydrated elderly patients: lokal effects with and without hyaluranidase A comparison of intravenous and subcutaneous hydration in elderly acute stroke patients (Challiner et al., 1994) Subcutaneous fluids in elderly hospital patients with cognitive impairment (O'keeffe & Lavan, 1996) Comparison of subcutaneous and intravenous rehydration in geriatric patients: a randomized trial (G. Slesak et al., 2003). Eficacia de la via subcutanea frente al la hidrataction intravenosa en el paciente anciano hospitalizado: estudio controlado aletorizado (Duems Noriega & Ariño Blasco, 2014) Is hypodermoclysis suitable for frail Chinese elderly? (JKH Luk, 2008)

Oversikt nr: 6	**Populasjon**	**Intervensjon**	**Sammen likning**	**Utfallsmål**	**Formål**
Subcutaneous fluid and drug delivery: safe efficient and inexpensive (Duems-Noriega & Ariño-Blasco, 2015)	Pasienter med dårlig venøs (i.v) tilgang eller som har en oral intoleranse. (Begge disse gruppene trenger en alternativ administrering av medisin og væsketilførsel.)	Subkutan administrering av væske og medikamenter.	Intravenøs behandling	Opptak av medikament og væske. Rehydrering målt ved Kreatinin nivå Osmolalitet Serum sodium + pasient ubehag.	Å lage en systematisk oversikt over bevisene for subkutan administrering av medikamenter og væske.
Konklusjon	Denne oversikten omtaler mest administrering av medikamenter subkutant. Men deres konklusjon ang subkutane væskebehandling er at det er et effektivt alternativ for rehydrering, av pasienter med mild til moderat dehydrering.				
Kritisk vurdering etter ROBIS (Whiting et al., 2016) Fase 1-3 Domene 1-4.	**Fase 1:** Den systematiske oversikten er delvis relevant for min PICO. Inneholder veldig lite om væskebehandling og masse om medikamenter. **Fase 2** **Domene 1**: Formålet var å lage en systematisk oversikt, men metodedelen er svært lite beskrevet. Ikke gjennomsiktig for leser. Beskriver ingen protokoll. Svært mangelfull beskrivelse av inklusjonskriteriene. Forfatterne skriver at de fulgte retningslinjene til " Institute of medicine" ang kriterier for funn og vurdering av studier ble med i studien. Og at de valgte ut studier uten begrensinger på år eller språk. Forfatterne beskriver ikke studiedesign på inkluderte studier i metodedel. **Domene 2:** Det er gjort søk i CINAHL, EMBASE, PubMed og Cochrane Library. Databasene er svært hensiktsmessig, men kunne også tatt søk i MEDLINE. Søkeord: MeSH: "Subcutaneous route, hypodermoclysis, ketoralac, morphine,cefotriaxone, analgetics, opioids, antibiotics" De beskriver ikke at de har gjort tekstordsøk. Søkestrategi ikke vedlagt. **Domene 3:** Metodene for dataekstrasjon og vurdering av studiene er ikke beskrevet. Det er ikke skrevet om bias i de inkluderte studiene annet enn at de fulgte retningslinjene til "institute of medicine". **Domene 4:** Metodene som ble brukt for å sammenfatte studiene er ikke beskrevet. De fant 178 artikler, men beskriver ikke hvor mange av dem som ble inkludert. De skriver at studiene var veldig heterogen, da alle studiene var fra primæromsorgen, sykehus, sykehjem og helsesentre. Og at det var stor variasjon i utvalgsstørrelsen til disse studiene. Videre beskrives det at studiene som var inkludert hadde bias på randomisering, forskjeller i grupper, og svært små utvalg. Det er ikke beskrevet noe om forhåndsdefinerte analyser Resultatene for rehydrering ble presentert i en tabell. 10 inkluderte studier. 5 RCT, 3 prospektiv, 1 retrospektiv og 1ukontrollert. Ingen oversikt om bias i de inkluderte studiene. **Fase 3:** Denne oversikten vurderes til å ha høy risiko for systematiske skjevheter.				

RCT studier i oversikten om rehydrering	• A comparison of intravenous and subcutaneous hydration in elderly acute stroke patients (Challiner et al., 1994). • Is hypodermoclysis suitahie for frail Chinese elderly?(JKH Luk, 2008). • Efficacy of the subcutaneous route compared to intravenous hydration in the elderly hospitalised patient: a randomised controlled study (Duems Noriega & Ariño Blasco, 2014). • Subcutaneous hydration in the elderly (O'Keeffe & Geoghegan, 2000) • Comparison of subcutaneous and intravenous rehydration in geriatric patients: a randomized trial (G. Slesak et al., 2003).

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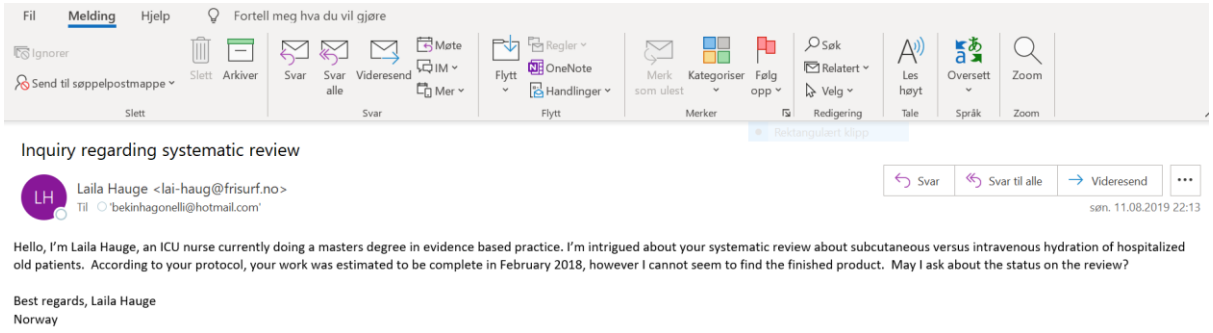
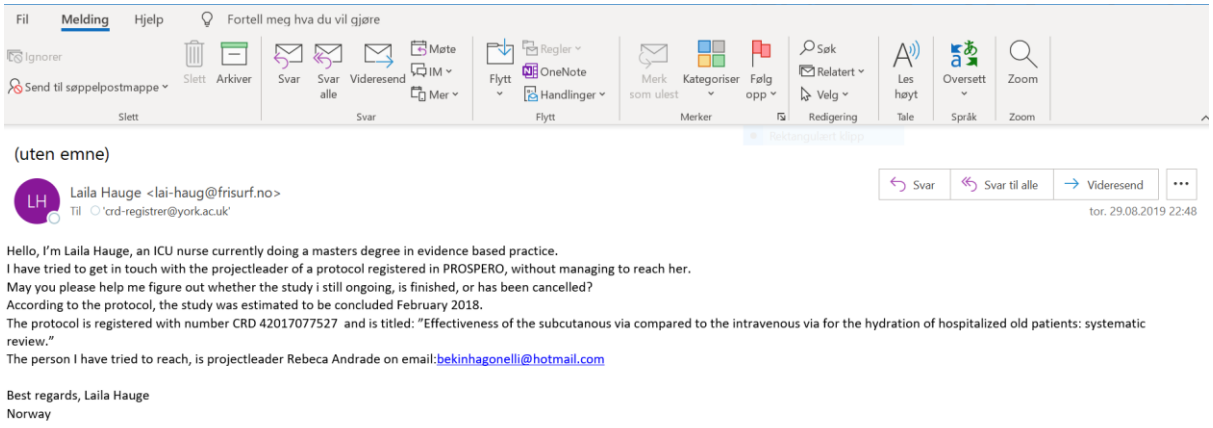
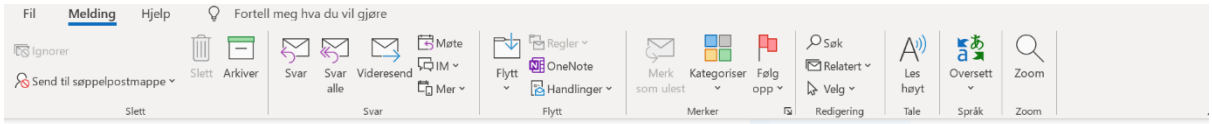
Appendix III Email request to a scientist in Brazil

Nedenfor viser vi til epostkorrespondanser mislykkede forsøk på å få tak i forfatterne av en protokoll som oppgav at studien deres, med samme tema som vårt, skulle vært ferdig februar 2018 Engelsk?







Re:

CR

CRD Register <crd-register@york.ac.uk>
Til Laila Hauge

Svar | Svar til alle | Videresend | ...

fre. 30.08.2019 11:00

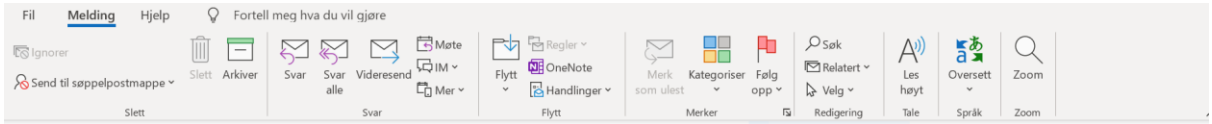
Hi there,

Unfortunately, we cannot chase up people regarding their reviews. We do not have the time or resources to be able to do this, and we explain that each record is the reviewer's responsibility. We can only suggest that you continue to contact her through the email given.

PROSPERO Admin team
Centre for Reviews and Dissemination
University of York
York
YO10 5DD
t: +44 (0) 1904 321049

www.york.ac.uk/inst/crd
www.crd.york.ac.uk/prospero/

On Fri, 30 Aug 2019 at 05:30, Laila Hauge <lai-haug@frisurf.no> wrote:



PROSPERO protocol "Effectiveness of the subcutaneous via compared to the intravenous via for the hydration of hospitalized old patients: systematic...

Birgitte Graverholt <Birgitte.Graverholt@hvl.no>
Til bekinhagonelli@hotmail.com

Svar | Svar til alle | Videresend | ...

tir. 03.09.2019 20:51

Hi and greetings from Norway –

You are listed as contact person for the protocol referred to above.

I have a question with regards to the protocol that you have published in PROSPERO, for the systematic review with the title: "**Effectiveness of the subcutaneous via compared to the intravenous via for the hydration of hospitalized old patients: systematic review**"

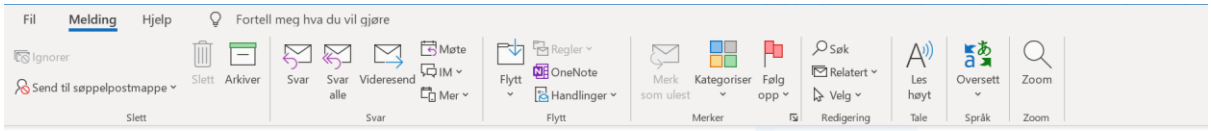
It says that anticipated completion date is February 28th 2018. Can you please estimate new completion date, or say something about the process you're at with this review? I am supervising a student that is interested in this same topic and she is considering a similar work.

Beste hilsen / Best wishes
Birgitte Graverholt

Senterleder – Head of Centre / Senter for kunnskapsbasert praksis – Centre for Evidence-Based Practice / Høgskulen på Vestlandet – Western Norway University of Applied Sciences
Tlf: +47 55 58 55 11 – 41 10 03 20 Besøksadresse: Inndalsveien 28, Bergen

Postboks 7030 5020 Bergen
www.hvl.no | twitter.com/hvl_no | facebook.com/hvl.no

Høgskulen på Vestlandet



PROSPERO protocol "Effectiveness of the subcutaneous via compared to the intravenous via for the hydration of hospitalized old patients: systematic..

Birgitte Graverholt <Birgitte.Graverholt@hvl.no>
Til imip@imip.org.br

Svar | Svar til alle | Videresend

tir. 03.09.2019 20:5

Hi to whoever at may concern, and greetings from Norway –

According to the information in PROSPERO, the authors of this review are listed as employees with IMIP. Can you please forward this email to the persons listed below? I have trouble finding their email addresses or contact information:

Review team members and their organisational affiliations

Mrs LARYSSA MARYSSAN. IMIP
Professor REBECA ANDRADE. IMIP
Dr MIRELLA REBELLO. IMIP
Professor FLÁVIA ORANGE. IMIP

I have a question with regards to the protocol that is published in PROSPERO, for the systematic review with the title: **"Effectiveness of the subcutaneous via compared to the intravenous via for the hydration of hospitalized old patients: systematic review"**

It says that anticipated completion date is February 28th 2018. Can you please estimate new completion date, or say something about the process you're at with this review? I am supervising a student that is interested in this same topic and she is considering a similar work.

Beste hilsen
Birgitte Graverholt

Appendix IV A protocol for å systematic review (published version)

Protocol for a systematic review:

Review title:

"The effect of subcutaneous fluid therapy versus intravenous fluid therapy on dehydration in elderly people in nursing homes."

Anticipated or actual start date:

This review was started January 2020

Anticipated completion date:

20.05.2021

Stage of review at time of this submission:

At this time, the question has been posed, a search-strategy constructed and we are about to conduct a search, and select studies.

Named contact:

Laila Hauge
Gro Holmelid

Named contact e-mail:

105069@stud.hvl.no
103735@stud.hvl.no

Organisational affiliation of the review:

Western Norway University of Applied Sciences
www.hvl.no

Review team members and their organisational affiliations:

Professor Hans Lund, Western University of Applied Sciences – Supervisor

Senior Researcher, Eva Marie-Louise Denison, Division of health services-Norwegian Institute of Public health – Supervisor

Funding sources/sponsors:

This project receives no funding.

Conflicts of interest:

No known conflicts of interest.

Collaborators:

No other partners.

We will work as a team and both will be active participants in the whole process.

Review question:

"What is the effect of subcutaneous fluid therapy versus intravenous fluid therapy on dehydration in elderly people in nursing homes."

Searches:

Systematic search for randomized clinical trials will be conducted via the databases of the following platforms: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL and Epistemonikos.

The search strategy will include different MeSh terms and textwords for dehydration and fluid therapy. The search terms will be adapted for use with other bibliographic databases in combination with other database-spesific filters for controlled trials, where these are available. The search strategy aims to find both published and unpublished studies. The reference list of all identified reports and articles will be searched for additional studies.
There will be restrictions for English and Scandinavian language, but not any restrictions relating to date of publishing. The searches will be re-run just before the final analyses and further studies retrieved for inclusion.

Condition or domain being studied:

One of the most frequent complications that affect the elderly population is dehydration, defined as the loss of body water and salts essential for normal body function due to pathological fluid losses, decreased water consumption or a combination of both.

Increased fluid intake and replacement of lost electrolytes are usually sufficient to restore fluid balances in patients who are mild or moderate dehydrated. For individuals who are mildly dehydrated, just drinking plain water may be all the treatment that is needed.

The oral route is considered of choice for hydration because it is easy to perform, physiological and non-invasive, but some circumstances (cognitive disturbances, swallowing changes, low level of consciousness), which are highly prevalent in the elderly, may make it difficult to use this route.

When the oral route can not be instituted, intravenous fluid treatment may be necessary and is most commonly used. In this case, absorption occurs immediately and the patient's response is rapid. However, it is not always possible, since the peripheral vessels of the elderly undergo physiological changes typical of aging, increasing the probability of bleeding and loss of access.

In addition, intravenous pathway is associated with some complications, such as increased risk of pulmonary edema and hyponatremia in patients with heart failure. It is worth mentioning that it may present as an uncomfortable, difficult to access, painful pathway associated with multiple punctures due to the capillary fragility of the elderly, immobilization of the punctured limb, risk of infection and thrombophlebitis.

In order to reduce these complications and mainly avoid the numerous attempts of venipuncture, the subcutaneous route has been increasingly used in patients with mild to moderate dehydration.

Type of study to be included:

Randomized controlled trials in the elderly, aged above 65 years, undergoing subcutaneous or intravenous therapy for the treatment of mild to moderate dehydration, will be included.

Participants/population:

Elderly population, aged above 65 years

Intervention/control:

The subcutaneous route will be compared with the intravenous route for the administration of fluids to treat mild to moderate dehydration in the elderly

population, over 65 years, in nursing homes. If there are few studies from nursing homes, we will consider to include studies from the hospital settings. The intervention group is those who receive subcutaneous fluid therapy regardless of fluid volume, fluid type and duration of treatment and the control group is those who receive intravenous fluid therapy, regardless of fluid type, amount and duration of treatment.

Main outcome:

The primary outcome studied will be hydration status.

Measures of effect:

Measured in osmolality, urea, mean arterial pressure (MAP) or other methods.

Additional outcome:

Secondary outcome is to look at complications for the two treatment methods.

Data extraction (selection and coding):

Titles and abstracts of studies retrieved using the search strategy and those from additional sources will be screened independently by two review authors to identify studies that potentially meet the inclusion criteria. The full text of these potentially eligible studies will be retrieved and independently assessed for eligibility by two review authors. Any disagrement between us over the eligibility of particular studies will be resolved through discussion with a supervisor.
The data will be retrieved by two independent persons using a data retrieval form, which will be created in advance. If disagreements arise, this will be resolved by discussion with each other and by including a supervisor. The data retrieved will be presented in a table. Data that will be relevant to retrieve are:

Country of study, number of participants in the intervention and control group, dropout rate, outcome measure and age, gender, effect measure and effect estimate.
The data retrieval form will be piloted (tested) by two different people. This helps to ensure data retrieval.

Risk of Bias (quality) assessment:

The Cochrane tool will be used to assess the risk of bias in randomized controlled trials. The evaluation of each trial will be carried out according to the following methodological quality domains:
sequence generation, allocation concealment, blinding of participants, personnel and outcomes assessors, incomplete outcome data, selective outcome reporting, and other sources of bias.
In this way, the risk of bias for each item will be classified as low, high or uncertain. The risk will be classified as low if all domains are evaluated as appropriate. On the other hand, it will be considered a high risk if one or more of the domains are evaluated as inappropriate or uncertain.

Strategy for data synthesis

We will try to assess heterogeneity among studies through visual inspection of the forest plots and the use of the I^2 statistic. If we identifiy significant heterogeneity we use a random-effects model, otherwise, we incorporate a fixed-effect model. We performe the meta-analysis using the Review Manager software program (RevMan 5).
For dichotomous outcomes we will calculate relative risks with 95% CIs.
Continuous data will be reported as mean differences (MDs) with 95% CIs.
A heterogeneity between 0-40% has little impact on the result as a certain variation between the included studies is desirable, based on the external validity.

30-60% is a moderate difference between the studies. 50% and above involves a significant difference that will affect the credibility of the results in the review.
In such cases with a high I2 score, a subgroup analysis or a meta-regression will be made.

If heterogeneity is very high (i.e. > 90%) we will report results narratively. If there are data from only one study for an outcome, the results will be reported narratively.
Furthermore a chart to summarize the results from the different studies will be made. Here the studies, effects on intervention and control groups and risk of bias, will be presented.

Type and method of review
Intervention , Meta-analysis, systematic review

Language:
English

Country:
This review is being carried out in Norway.

Details of any existing review of the same topic by the same authors:

No review of the same topic by the same authors exist.

Current review status:
Review ongoing

Appendix V Keywords and search strategies

	P: Dehydration in the elderly obove 65 years in nursing homes	I: Subcutanous fluid treatment C: Intravenous fluid treatment
Searchterms in Epistemonikos		
Keywords in Cochrane Library	Water-elektrolyte imbalance *(Emneordet inkluderer "dehydration")* Water loss, insensible	Fluid Therapy Infusions, Subcutaneous Infusions, Parenteral Infusions, intravenous Administration, intravenous Hypodermoclysis Rehydration, solutions
Keywords in MEDLINE	Water-elektrolyte imbalance *(Emneordet inkluderer "dehydration")* Water loss, insensible	Fluid Therapy Infusions, Subcutaneous Infusions, Parenteral Infusions, intravenous Administration, intravenous Hypodermoclysis Rehydration, solutions
Keywords in EMBASE	Dehydration	Fluid Therapy Infusions, Subcutaneous Infusions, Parenteral Infusions, intravenous Administration, intravenous Hypodermoclysis Rehydration, solutions
Keywords in CINAHL	Fluid- elektrolyte imbalance	Fluid therapy Intravenous therapy

	Water loss, Insensible	
Textwords:	Dehydration Fluid-elektrolyte imbalance Water loss, Insensible Dehydration Dehydrated Water Stress Stress, Water Drying up Drying out Fluid deprivation Deprivation of water Fluid loss Loss of body water Decrease in total body fluid. Reduction of water content Exsiccation Cellular desiccation Anhydration Hypodration Enhydration Volunary dehydration Hypercalcemia Hypercalcciuria Hyperkalemia Hypermagnesemia Hypernatremia Hyperphosphatemia Hypophosphatemia	Fluid therapy Fluid resuscitation Therapy, Fluid Fluid Therapies Therapies, Fluid Rehydration Rehydrations Rehydration, solutions Infusions, intravenous Infusions, parenteral Infusions, subcutaneous Hypodermoclyses Hypodermoclysis Administration, intravenous Administration, subcutaneous Fluid

	Inappropriate ADH Syndrome Refeeding Syndrome Water intoxication	
Non relevante words:	Loss of electrolytes Hypocalcemia Hypokalemia Hypomagnesemia Hyponatremia	Oral Rehydration Therapy Therapy, Oral Rehydration Rehydration Therapy, Oral Oral Rehydration Therapies Rehydration Therapies, Oral Therapies, Oral Rehydration Oral Rehydration Oral Rehydrations Rehydrations, Oral Rehydration, Oral

Search in Cochrane Library

```
Search Name:    Masteroppgave i KBP Søkedato 290820
Date Run:       13/12/2020 17:44:39
Comment:

ID      Search  Hits
#1      MeSH descriptor: [Water Loss, Insensible] explode all trees     285
#2      MeSH descriptor: [Water-Electrolyte Imbalance] explode all trees
1694
#3      (dehydrat*):ti,ab,kw OR (water NEXT stress):ti,ab,kw (Word variations
have been searched)     3283
#4      (Water NEXT Electrolyte NEXT Imbalance):ti,ab,kw OR (Insensible NEXT
Water NEXT Loss):ti,ab,kw OR (Fluid NEXT Elektrolyte NEXT Imbalance):ti,ab,kw OR
(Drying NEXT (up OR out)):ti,ab,kw OR (Fluid NEXT deprivation*):ti,ab,kw
181
#5      (deprivation* NEXT of NEXT water):ti,ab,kw OR (Fluid NEXT loss):ti,ab,kw
OR (Loss NEXT of NEXT body NEXT water):ti,ab,kw OR (Decrease NEXT in NEXT total
NEXT body NEXT fluid):ti,ab,kw OR (Reduction NEXT of NEXT water NEXT
content):ti,ab,kw       181
#6      (exsoccation*):ti,ab,kw OR (cellular NEXT desiccation*):ti,ab,kw OR
(anhydration*):ti,ab,kw OR (hypodration*):ti,ab,kw OR (enhydration*):ti,ab,kw
0
#7      (volunary NEXT dehydrat*):ti,ab,kw OR (Hyper NEXT (calcemia OR
calcciuria OR kalemia OR magnesemia OR natremia OR phosphatemia)):ti,ab,kw
5
#8      (inappropriate NEXT ADH NEXT syndrome):ti,ab,kw OR (refeeding NEXT
syndrome):ti,ab,kw OR (water NEXT intoxication):ti,ab,kw        95
#9      #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8    4908
#10     MeSH descriptor: [Hypodermoclysis] explode all trees    15
#11     (hypodermoclys*):ti,ab,kw OR (infusion*):ti,ab,kw OR (subcutaneous NEXT
(fluid or hydration*)):ti,ab,kw (Word variations have been searched)     67796
#12     MeSH descriptor: [Fluid Therapy] explode all trees      1684
#13     MeSH descriptor: [Infusions, Subcutaneous] explode all trees    153
#14     MeSH descriptor: [Infusions, Parenteral] explode all trees      12410
#15     MeSH descriptor: [Infusions, Intravenous] explode all trees     10270
#16     MeSH descriptor: [Administration, Intravenous] explode all trees
18586
#17     MeSH descriptor: [Rehydration Solutions] explode all trees      293
#18     (hypodermoclys*):ti,ab,kw       34
#19     (infusion*):ti,ab,kw OR (Fluid NEXT resuscitation*):ti,ab,kw    68456
#20     (Subcutaneous NEXT fluid NEXT Administration*):ti,ab,kw OR (subcutaneous
NEXT hydration*):ti,ab,kw OR (Rehydrat*):ti,ab,kw OR (Fluid NEXT
therap*):ti,ab,kw       4032
#21     (intravenous):ti,ab,kw  87056
#22     #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR
#20 OR #21      125898
#23     #9 AND #22      1632
#24     randomized NEXT controlled NEXT trial   867075
#25     RCT     34400
#26     #24 OR # 25     955952
#27     #23 AND #26     1221
```

Search in MEDLINE

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to 24 nov, 2020>

Search Strategy:

---

1 exp Dehydration/ (13655)

2 exp Water-Electrolyte Imbalance/ (62913)

3 exp Water Loss, Insensible/ (2393)

4 dehydrat*.tw. (44632)

5 Water-Electrolyte Imbalance.tw. (113)

6 water loss insensible.tw. (0)

7 water stress.tw. (4558)

8 drying up.tw. (157)

9 drying out.tw. (181)

10 fluid deprivation.tw. (205)

11 fluid loss.tw. (1333)

12 loss of body water.tw. (86)

13 decrease in total body fluid.tw. (2)

14 reduction of water content.tw. (64)

15 exiccation.tw. (0)

16 cellular desiccation.tw. (10)

17 anhydration.tw. (6)

18 hypodration.tw. (0)

19 enhydration.tw. (0)

20 volunary dehydration.tw. (0)

21 hypercalcemia.tw. (13588)

22 hypercalcciuria.tw. (0)

23 hyperkalemia.tw. (6194)

24 hypermagnesemia.tw. (510)

25 hyperphosphatemia.tw. (3475)

26 hypophosphatemia.tw. (3777)

27 inappropriate ADH syndrome.tw. (27)

28 refeeding syndrome.tw. (452)

29 water intoxication.tw. (887)

30 or/1-29 (123381)

31 exp Fluid Therapy/ (20843)

32 exp Infusions, Subcutaneous/ (1255)

33 exp Infusions, Parenteral/ (93428)

34 exp Infusions, Intravenous/ (55692)

35 exp Administration, Intravenous/ (145302)

36 exp Hypodermoclysis/ (135)

37 exp Rehydration Solutions/ (1473)

38 fluid therapy.tw. (3607)

39 hypodermoclysis.tw. (133)

40 infusion fluid.tw. (281)

41 infusion liquid.tw. (29)

42 intravenous fluid.tw. (2843)

43 fluid resuscitation.tw. (5343)

44 fluid therap*.tw. (3639)

45 rehydration*.tw. (8403)

46 infusion* intravenous.tw. (182)

47 infusion* parenteral.tw. (7)

48 infusion* subcutaneous.tw. (21)

49 hypodermoclys*.tw. (134)

50 administration intravenous.tw. (307)

51 administration subcutaneous.tw. (105)

52 or/31-51 (212581)

53 exp Randomized Controlled Trial/ (532139)

54 ((random* and (controlled or control or placebo or versus or vs or group or groups or comparison or compared or arm or arms or crossover or cross-over) and (trial or study)) or ((single or double or triple) and (masked or blind*))).tw. (788815)

55 53 or 54 (952172)

56 30 and 52 and 55 (798)

****

Search in EMBASE

EMBASE søk 10 oktober 2020

# ▲	Searches	Results	Type	
1	Dehydration/	13409	Advanced	More
2	dehydration/	13409	Advanced	More
3	dehydrat*.tw.	43672	Advanced	More
4	fluid-electrolyte imbalance.tw.	23	Advanced	More
5	water loss insensible.tw.	0	Advanced	More
6	water stress.tw.	4371	Advanced	More
7	drying up.tw.	153	Advanced	More
8	drying out.tw.	175	Advanced	More
9	fluid deprivation.tw.	204	Advanced	More
10	fluid loss.tw.	1304	Advanced	More
11	loss of body water.tw.	84	Advanced	More
12	decrease in total body fluid.tw.	2	Advanced	More
13	reduction of water content.tw.	60	Advanced	More
14	exiccation.tw.	0	Advanced	More
15	cellular desiccation.tw.	10	Advanced	More
16	anhydration.tw.	6	Advanced	More
17	hypodration.tw.	0	Advanced	More
18	enhydration.tw.	0	Advanced	

				More
☐	19	volunary dehydration.tw.	0	Advanced More
☐	20	hypercalcemia.tw.	13393	Advanced More
☐	21	hypercalcciuria.tw.	0	Advanced More
☐	22	hyperkalemia.tw.	6022	Advanced More
☐	23	hypermagnesemia.tw.	496	Advanced More
☐	24	hyperphosphatemia.tw.	3378	Advanced More
☐	25	hypophosphatemia.tw.	3676	Advanced More
☐	26	inappropriate ADH syndrome.tw.	27	Advanced More
☐	27	refeeding syndrome.tw.	431	Advanced More
☐	28	water intoxication.tw.	883	Advanced More
☐	29	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28	81683	Advanced More
☐	30	fluid therapy/	20361	Advanced More
☐	31	hypodermoclysis/	129	Advanced More
☐	32	infusion fluid/	0	Advanced More
☐	33	fluid therapy.tw.	3488	Advanced More
☐	34	hypodermoclysis.tw.	131	Advanced More
☐	35	infusion fluid.tw.	276	Advanced More
☐	36	infusion liquid.tw.	23	Advanced More

☐	37	intravenous fluid.tw.	2757	Advanced More
☐	38	fluid resuscitation.tw.	5188	Advanced More
☐	39	fluid therap*.tw.	3518	Advanced More
☐	40	rehydration*.tw.	8239	Advanced More
☐	41	infusion* intravenous.tw.	181	Advanced More
☐	42	infusion* parenteral.tw.	7	Advanced More
☐	43	infusion* subcutaneous.tw.	21	Advanced More
☐	44	hypodermoclys*.tw.	132	Advanced More
☐	45	administration intravenous.tw.	302	Advanced More
☐	46	administration subcutaneous.tw.	102	Advanced More
☐	47	30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	33155	Advanced More
☐	48	29 and 47	5410	Advanced More

Search in Epistemonikos

Epistimonikos søkestrategi, masteroppgave i KBP, 22 nov 2020

(title:(dehydrat*) OR abstract:(dehydrat*)) OR (title:(water stress) OR abstract:(water stress)) OR (title:(water electrolyte imbalance) OR abstract:(water electrolyte imbalance)) OR (title:(water loss insensible) OR abstract:(water loss insensible)) OR (title:(fluid electrolyte imbalance) OR abstract:(fluid electrolyte imbalance)) OR (title:(drying (up OR out)) OR abstract:(drying (up OR out))) OR (title:(fluid deprivation*) OR abstract:(fluid deprivation*)) OR (title:(deprivation* water) OR abstract:(deprivation* water)) OR (title:(fluid loss) OR abstract:(fluid loss)) OR (title:(loss of body water) OR abstract:(loss of body water)) OR (title:(decrease in total body fluid) OR abstract:(decrease in total body fluid)) OR (title:(reduction of water content) OR abstract:(reduction of water content)) OR (title:(hyper (calcemia OR calcciuria OR kalemia OR magnesemia OR natremia OR phosphatemia)) OR abstract:(hyper (calcemia OR calcciuria OR kalemia OR magnesemia OR natremia OR phosphatemia))) OR (title:(inappropriate ADH syndrome) OR abstract:(inappropriate ADH syndrome)) OR (title:(refeeding syndrome) OR abstract:(refeeding syndrome)) OR (title:(water intoxication) OR abstract:(water intoxication)) AND (title:(hypodermoclys*) OR abstract:(hypodermoclys*)) OR (title:(subcutaneous (fluid OR hydration*)) OR abstract:(subcutaneous (fluid OR hydration*))) OR (title:(Fluid therap*) OR abstract:(Fluid therap*)) OR (title:(infusions (subcutanious OR parenteral OR intravenous)) OR abstract:(infusions (subcutanious OR parenteral OR intravenous))) OR (title:(administration (intravenous OR subcutaneous)) OR abstract:(administration (intravenous OR subcutaneous))) OR (title:(rehydration solution*) OR abstract:(rehydration solution*)) OR (title:(hypodermoclys*) OR abstract:(hypodermoclys*)) OR (title:(infusion*) OR abstract:(infusion*)) OR (title:(fluid resurcitation*) OR abstract:(fluid resurcitation*)) OR (title:(subcutaneous hydration*) OR abstract:(subcutaneous hydration*)) OR (title:(rehydrat*) OR abstract:(rehydrat*)) OR (title:(intravenous) OR abstract:(intravenous))

Treff: 14

Fikk ikke noen treff på følgende ord: (Er derfor blitt utelatt i søkestrategi)

- Exsoccation
- Cellular desiccation
- Anhydration
- Enhydration
- hypodration

Search in CINAHL

EBSCOhost

Monday, November 16, 2020 1:06:42 PM

#	Query	Limiters/Expanders	Last Run Via	Results
S23	S14 AND S22	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	2,248
S22	S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	26,050
S21	AB administration intravenous OR AB administration subcutaneous fluid	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	2,009
S20	AB infusions parenteral OR AB infusions subcutaneous OR AB hypodermoclys*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	358
S19	AB fluid resuscutation OR AB rehydrat* OR AB infusions intravenous	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	3,845
S18	AB fluid therap* OR AB Intravenous therap* OR AB Fluid intake output-measur*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	1,516
S17	(MH "Fluid Intake-Output Measures")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	478
S16	(MH "Intravenous Therapy+")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases Search Screen - Advanced	12,667

		Search modes - Boolean/Phrase	Search Database - CINAHL	
S15	(MH "Fluid Therapy+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	19,402
S14	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	20,675
S13	AB water intoxication	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	63
S12	AB hypophosphatemia OR AB inappropriate ADH syndrome OR AB refeeding syndrome	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	711
S11	AB hypermagnesemia OR AB hypernatremia OR AB hyperphosphatemia	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	1,079
S10	AB hypercalcemia OR AB hypercalcciuria OR AB hyperkalemia	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	2,709
S9	AB hypodration OR AB enhydration OR AB volunary dehydration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	0
S8	AB hypodration OR AB enhydration OR AB volunary dehydration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	0
S7	AB exsiccation OR AB cellular desiccation OR	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases	0

	AB anhydration	Search modes - Boolean/Phrase	Search Screen - Advanced Search Database - CINAHL	
S6	AB loss of body water OR AB decrease in total body fluid OR AB reduction of water content	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	42
S5	AB fluid deprivation OR AB Deprivation of water OR AB fluid loss	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	406
S4	AB water stress OR AB drying up OR AB drying out	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	50
S3	AB fluid-electrolyte imbalance OR AB water loss insensible OR AB dehydrat*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	4,133
S2	(MH "Water Loss, Insensible")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	131
S1	(MH "Fluid-Electrolyte Imbalance+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	15,326

Appendix VI Peer Review of Electronic Search Strategies (PRESS)

(Written in norwegian by our librarian)

Peer Review of Electronic Search Strategies (PRESS)			
Review title: The effect of subcutaneous fluid therapy versus intravenous fluid therapy on dehydration in the elderly people in nursing homes			
Student: Laila Hauge og Gro Holmelid.		**Reviewer:** Gøril Tvedten Jorem	**Date completed:** 16.12.2020
Database: Cochrane, Embase, Cinahl og Epistemonikos.			
			If "B" or "C," please provide an explanation or example:
1	**Translation of the research question**	☒ A. No revisions ☐ B. Revision(s) suggested ☐ C. Revision(s) required	Ble litt usikker på aspektet med Population ved det jeg tolker som problemstillingen deres – er det slik at dere vil fokusere på eldre over 65 år i sykehjem? Er det aktuelt å prøve å avgrense søkene deres til f.eks. eldre over 65 år?
2	**Boolean and proximity operators**	☐ A. No revisions ☒ B. Revision(s) suggested ☐ C. Revision(s) required	I Cinahl og Embase er det mulig å bruke nærhetsoperatører når dere søker etter tekstord. Er ikke et must, men dere kan jo vurdere det? Se denne bloggen her for info om nærhetsoperatører i Cinahl og andre baser: https://litteratursok.blogspot.com/2018/10/veien-gjennom-jungelen.html (Under overskriften «Databasene» velger dere aktuell database. Der finner dere både nærhetsoperatører og eventuelt andre søketips). Ser at dere har brukt nærhetsoperatører i Cochrane-søket deres.
3	**Subject headings**	☒ A. No revisions ☐ B. Revision(s) suggested	

		☐ C. Revision(s) required	
4	**Text word searching**	☐ A. No revisions ☒ B. Revision(s) suggested ☐ C. Revision(s) required	I Epistemonikos: Det er mulig å sette ord som består av flere ord (fraser) i anførselstegn ("xy"). Om dere ikke bruker anførselstegn tolker basen det som and – altså at f.eks. water AND stress står et sted i artikkelen. Ved å bruke anførselstegn tvinger dere basen til å søke etter treff hvor disse to ordene står ved siden av hverandre. Kan det være aktuelt for dere å bruke? I Cinahl: hvorfor søker dere kun i abstract etter tekstord? Er det aktuelt å søke i f.eks. tittel-feltet også? I Cinahl – som i Epistemonikos – er det greit å bruke anførselstegn når dere søker etter noe som består av flere ord. Hvis ikke finner den water et sted i abstract og stress et annet sted. Se for øvrig tips om bolske operatører under avsnitt 2 lengre oppe. I Embase-søket deres ville jeg kanskje dobbeltsjekket hvorfor dere får 0 treff på enkelte av tekstordsøkene deres. Skrev inn water loss insensible.tw. akkurat som dere gjorde, og fikk 5 treff. Når jeg brukte nærhetsoperatøren adj1 slik: (water adj1 loss adj1 insensible).kw. fikk jeg 19 treff. Se nærmere på søk 11, 12 og 13 – er det mulig å bruke nærhetsoperatører eller annet i stedet for et eller flere ord her?
5	**Spelling, syntax, and line numbers**	☐ A. No revisions ☒ B. Revision(s) suggested ☐ C. Revision(s) required	I Embase: Exiccation ser ut til å være stavet feil – skal det være en s der? Exsiccation. Ser ut som om det var et par andre ord som var skrevet feil også. Sjekk spesielt de søkene dere har gjort som får 0 eller svært få treff. Exsiccation ser ut til å være skrevet riktig i Cochrane-søket deres. Pass på at dere «oversetter» søket fra en base til en annen riktig, at dere gjør det samme i alle baser (men selvfølgelig ta høyde for forskjellene i søkefunksjoner mellom basene), da får dere treff på samme emne i alle basene.
6	**Limits and filters**	☐ A. No revisions ☒ B. Revision(s) suggested	Har dere vurdert å avgrense søket i f.eks. Cinahl og Cochrane hvor dere får en del treff? F.eks. på språk eller publikasjonsdato? Eventuelt også inkludere et tredje aspekt i søket – eldre over 65 år? Er det forskjell på væskebehandling en gir eldre over 65 år som sliter med dehydrering i forhold til voksne under 65 år? Har sykehjem emne rutiner på dette, eller må de ta hensyn til andre aspekter?

		☐ C. Revision(s) required	
7	**Overall evaluation** (if one or more «revision required is noted above, the response must be «revisions required»)	☒ A. No revisions ☐ B. Revision(s) suggested ☐ C. Revision(s) required	Søket ser veldig bra ut! Dere kan jo faget bedre enn meg, men ser ut som om dere har fått med dere relevante termer. Logisk bygget opp, og riktig bruk av OR og AND. Har kun et par forslag/spørsmål som dere eventuelt kan vurdere (se over), men generelt ser søket veldig bra ut!

Appendix VII Excluded studies

22 excluded studies and the reasons why in the table below.

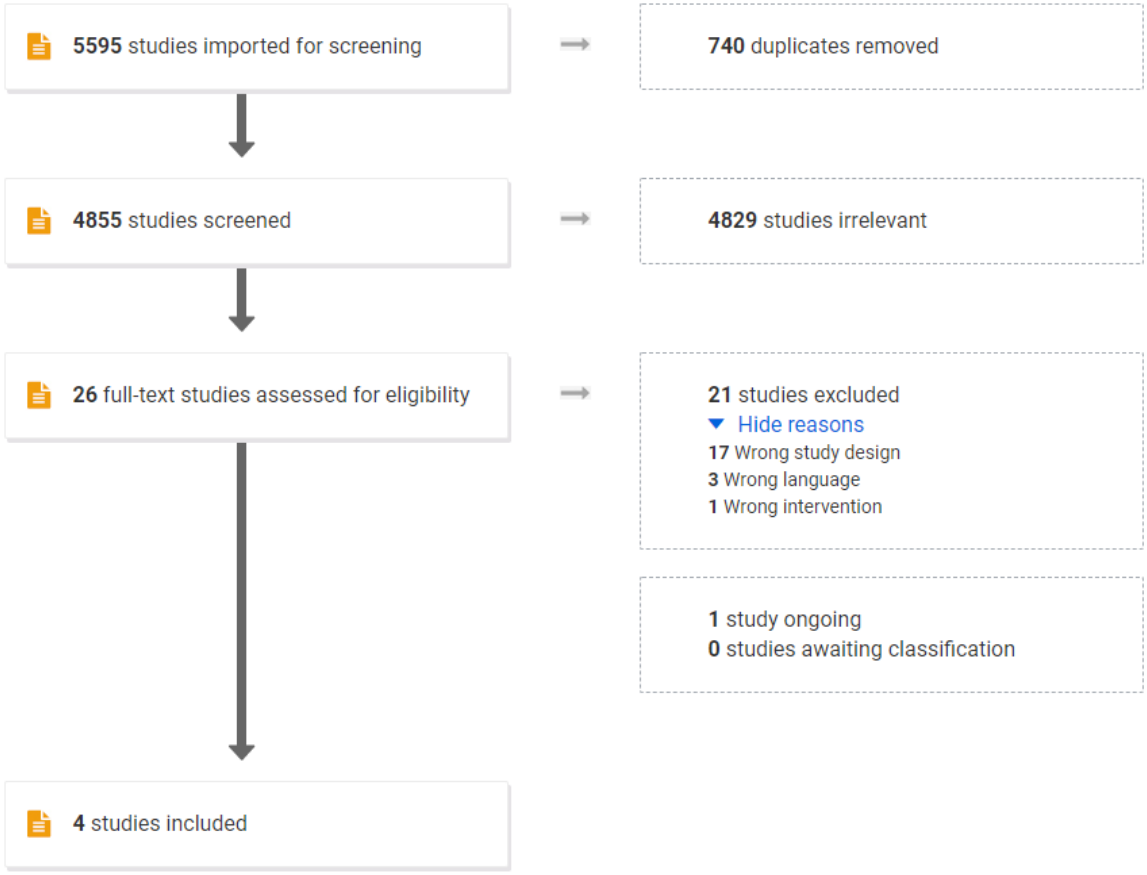
Name of the study	Reason for exclusion
(Arinzon et al., 2004) ***Hypodermoclysis (subcutaneous infusion) effective mode of treatment of dehydration in long-term care patients.***	Wrong study design.
(Feinsod et al., 2004) ***Dehydration in frail, older residents in long-term care facilities***	Wrong study design. This is a literature review. This article is the first in a series of three articles that are dedicated to hydration issues in LTC. It focuses on the important scientific and medical basis for managing fluid and electrolyte balance.

(Eduardo et al., 2015) ***Canalization of a subcutaneous route as a valid alternative for geriatric patients in hospital stay with moderate dehydration.***	Wrong study design. We did not find this study, only title and abstract. Our librarian didn´t find it either.
(Lybarger, 2009) ***Hypodermoclysis in the home and long-term care settings.***	Wrong study design. Review of the literature.
(Dasgupta et al., 2000) ***Subcutaneous fluid infusion in a long-term care setting.***	Wrong study design. This study is a prospective observational study where the objective is to study the use of hypodermoclysis in a long-term care setting for chronic fluid supplementation and to compare it to intravenous (IV) fluid in the treatment of acute mild to moderate dehydration.
(Feinsod et al., 2004) ***Dehydration in frail, older residents in long-term care facilities***	Same as the one above from 2002.
(Dainty & Jimmy, 2009) ***Subcutaneous fluids--a blast from the past or a rosy future?***	Wrong study design. This review considers some of the clinical and practical issues associated with this method of fluid administration, and its role in contemporary health care.
(Barreto Annes et al., 2020) ***Subcutaneous Versus Intravenous Rehydration in Hospitalized Older Adults: A Meta-Analysis***	Wrong study design. This is a meta-analysis of three RCT`s that we have considered. Two of them are met our inclusion criteria and is in our SR.
(Remington & Hultman, 2007) ***Hypodermoclysis to treat dehydration: a review of the evidence.***	Wrong study design. This article reviews the relevant literature on the use of HDC to treat mild to moderate dehydration in older adults.
(Sasson & Shvartzman, 2001)	Wrong study design. Literature review.

Hypodermoclysis: An alternative infusion technique	An article that presents the advantages and disadvantages of the technique of hypodermoclysis.
(Constans et al., 1991) ***Hypodermoclysis in dehydrated elderly patients: local effects with and without hyaluronidase***	Wrong intervention. In this study Hyaluronidase were added to the solution infused subcutaneously. The local effects of hypodermoclysis with or without hyaluronidase were investigated by using a randomized double-blind study in 12 dehydrated elderly patients.
(Rochon et al., 1997) ***A systematic review of the evidence for hypodermoclysis to treat dehydration in older people.***	Wrong study design. This is a SR, containing 18 studies were 2 are RCT`s. Both RCT`s have been taken into concideration in our systematic review.
(Caccialanza et al., 2018) ***Subcutaneous Infusion of Fluids for Hydration or Nutrition: A Review.***	Wrong study design. In this review, the authors provide an overview of the technique, summarize findings from studies that have examined the use of subcutaneous infusion of fluids for hydration or nutrition, and describe the indications, advantages, and disadvantages of subcutaneous infusion.
(Frisoli Junior et al., 2000) ***Subcutaneous hydration by hypodermoclysis. A practical and lowcost treatment for elderly patients.***	Wrong study design. Review article that evaluates the evidence supporting the use of hypodermoclysis to treat elderly patients with dehydration and patients with terminal cancer, and discusses its indications, adverse effects and perspectives. A MEDLINE search of the last 30 years was done to recover all available literature.
(Lopez & Reyes-Ortiz, 2010) ***Subcutaneous hydration by hypodermoclysis***	Wrong study design. We did not find this article in fulltext, but according to the abstract we exclude it because of wrong design.
(Goncalves & Pimentel, 1998) ***Hipodermoclysis***	Wrong language. This article was written in Spanish/Portuguese.
(Duems Noriega & Ariño Blasco, 2014) ***Efficacy of the subcutaneous route compared to intravenous hydration***	Wrong language. This article was written in Spanish.

in the elderly hospitalised patient: a randomised controlled study.	
(Farrand & Campbell, 1996) ***Safe, simple subcutaneous fluid administration***	Wrong study design. We did not find this article in fulltext, but according to the abstract we exclude it because of wrong design.
(Danielsen et al., 2020) ***Harms and Benefits of Subcutaneous Hydration in Older Patients: Systematic Review and Meta-Analysis***	Wrong study design
(Dardaine et al., 1999) ***Subcutaneous infusion or hypodermoclysis: A useful rehydration technique in geriatrics***	Wrong language. This article is written in French.
(Mei & Auerhahn, 2009) ***Hypodermoclysis: maintaining hydration in the frail older adult.***	Wrong study design. Review article that evaluates the evidence supporting the use of hypodermoclysis to treat elderly patients with dehydration.
(Nct, 2018) **Subcutaneous vs Intravenous Hydration on Older Adults**	Ongoing study

Appendix VIII Flow chart



Appendix IX Characteristics of the included studies

Study, year	Country	Setting	Population	I and C	Outcome	Duration of treatment	Design
Challinger 1994	United Kingdom	Hospital setting, elderly care unit	34 acute stroke patients with a mean age of 83,5. Male 23, female 11. Dehydrated.	Intervention: Subcutenous fluid therapy. 2 liters of fluid per 24 h delivered through a butterfly needle. Comparison: Intravenous fluid therapy. 2 liters of fluid per 24 h through an IV access.	Primary oc:Serum osmolalities, mean s-osmolality 296 mOsm/kg at baseline. Secondary oc: Adverce effects. 2 minor erythema in the sc group and 1 bruising in the iv-group.	48 hours	Randomised controlled study

O`Keeffe, 1996	United Kingdom	Hospital setting, acute geriatric unit	60 geriatric patients with cognitive impariment. With a mean age of 82,5. Male 23, female 37 Mild dehydration or poor oral intake.	Intervention: SC fluid therapy. Up to 2 liters of fluid per 24 h with butterfly needle. Comparison: Intravenous fluid therapy through IV access, up to 2 liters fluid per 24 hours	Primary outcome: , Serum creatinin, mean 109,5 umol/l at baseline Secondary oc: Adverce effects. 2 local oedema in sc group and 0 in iv group.	48 hours	Randomised controlled study
Slesak, 2003	German (written in english)	Hospital setting, Geriatric ward in the Geriatric department	96 geriatric patients, mean age 85,3. Male 29, female 67. Mild to moderate dehydrated	Intervention: Subcutanous fluid therapy, up to 1,5 liters fluid per 24 h.Comparison: Intravenous fluid therapy, up to 1,5 liters per 24 hours.	Primary outcome: Sodium, mean 137 mmol/l at baseline. Secondary oc: Adverce effects.	6 days	Randomised controlled study

Appendix X Risk of bias assessment with RoB 2.0

Cochrane risk-of-bias tool for randomized trials.

Study ID: O`Keeffe, Outcome: Adverse effects

Unique ID	Gro Holmelid & Laila Hauge	**Study ID**	O`Keeffe 1996	**Assessor**	
Ref or Label		**Aim**	adhering to intervention (the 'per-protocol' effect)	**The effect of adhering to intervention…**	non-adherence to their assigned intervention by trial participants
Experimental	Subcutaneous fluid hydration	**Comparator**	Intravenous fluid hydration	**Source**	Journal article(s)
Outcome	Adverse effects	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	The allocation was decided by clinicians after meeting the inclusion criteria. Envelopes was concealed
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	There where no significance differences in the baselined characteristics of the two groups. The age mean, percent ladies,percent agitation and mean serum bloodsample is very simular and is not so different in the to groups. Tabel of random numbers were used to create blocks of 6 patients, 3 of whom were receiving eath treatment.
	Risk of bias judgement	**High risk**	High risk because the allocation was decided by clinicans and not random.
Bias due to deviations from intended interventions	2.1 Were participants aware of their assigned intervention during the trial?	Y	The treatment was not blinded for any of the groops because of its nature.
	2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	

	2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?	NA	
	2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	NA	
	2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	N	Two participants have dropt out and has been excluded in the analysis. This is å very low drop out rate and will not effect the outcome.
	2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Only two missing participants in the analysis. More than 95% data of the participants where available.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	There are no information on how the adverce effects are measured.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	NI	It is likely that the the way of measurment is the same in both groups but here is no information about this.
	4.3 Were outcome assessors aware of the intervention received by study participants?	NI	
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NI	there are no information about the outcome assessor.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NI	

	Risk of bias judgement	**High**	
	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	
Bias in selection of the reported result	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	
	5.3 ... multiple eligible analyses of the data?	NI	
	Risk of bias judgement	**High**	
Overall bias	**Risk of bias judgement**	**High**	

Study ID: Challiner 1994, Outcome: Hydration station

Unique ID	Gro Holmelid & Laila Hauge	**Study ID**	Challiner 1994	**Assessor**	
Ref or Label		**Aim**	adhering to intervention (the 'per-protocol' effect)	**The effect of adhering to intervention…**	non-adherence to their assigned intervention by trial participants
Experimental	Subcutaneous fluid hydration	**Comparator**	Intravenous fluid hydration	**Source**	Journal article(s)
Outcome	Hydration status	**Results**		**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Randomized using a computer. Block randomization was used with 8 patients in each block where 4 pasients are randomly assigned to the intervention group and the last 4 in the block are randomly assigned to the control group. The allocation was hidden with sealed envelopes that were not opened until the patient had agreed to
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	

			participate in the study. The envelopes were opened by the doctor on duty after the participants had been assigned to a group.
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	No. At baseline, 17 participants had been randomized to each group.
	Risk of bias judgement	**Low**	The randomization process is done correctly.
Bias due to deviations from intended interventions	2.1 Were participants aware of their assigned intervention during the trial?	Y	The treatment was not blinded for any of the groops because of its nature.
	2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?	Y	All participants recived the intended intervention
	2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	N	
	2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	PN	There were two dropouts in the subcutaneous group. One died and one developed local oedema. A proportion of less than 5 % is regarded as small and will not likely affect the outcome
	2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?		
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	The number of participants of missing outcome data is sufficiently small that their outcomes could have made no important difference to the estimated effect of intervation.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?		

	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		
	Risk of bias judgement	**Low**	The number of participants of missing outcomedata is sufficiently small that their outcomes coult have made no important difference to the estimated effect of intervation
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	The measuring was appropriate for this outcome.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	They measured serum osmolalitet i both groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?	NI	Outcome assessors could be blinded for the intervention recived, but there is no information about this.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	No it is a bloodsample.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	We have not seen any protocoll to this study, but the authors deskribes the prespecifides analysis plan in the article. The analysisdata do not raise any conserns. It is a blod sample that is not likely to be tampered with.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PY	The authors have left out dataanalysis of serum urea, glucose and elektrolites. They have only done an analysis of osmolalities.
	5.3 ... multiple eligible analyses of the data?	PY	The eligible reported results for the outcome measurement correspond to intended analysis.
	Risk of bias judgement	**High**	
Overall bias	**Risk of bias judgement**	**High**	The study is judged to be at high risk of bias in at least one domain for this result.

Study ID: Challiner 1994, Outcome: Adverse effects

Unique ID	Gro Holmelid & Laila Hauge	**Study ID**	Challiner 1994	**Assessor**	
Ref or Label		**Aim**	adhering to intervention (the 'per-protocol' effect)	**The effect of adhering to intervention…**	non-adherence to their assigned intervention by trial participants
Experimental	Subcutaneous fluid hydration	**Comparator**	Intravenous fluid hydration	**Source**	Journal article(s)
Outcome	Adverse effects	**Results**		**Weight**	1

Domain	Signalling question	Response	Comments
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Randomized using a computer. Block randomization was used with 8 patients in each block where 4 pasients are randomly assigned to the intervention group and the last 4 in the block are randomly assigned to the control group. The allocation was hidden with sealed envelopes that were not opened until the patient had agreed to participate in the study. The envelopes were opened by the doctor on duty after the participants had been assigned to a group.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	No. At baseline, 17 participants had been randomized to each group.
	Risk of bias judgement	**Low**	The randomization process is done correctly.
Bias due to deviations from intended interventions	2.1 Were participants aware of their assigned intervention during the trial?	Y	The treatment was not blinded for any of the groops because of its nature.
	2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	

	2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?	Y	All participants recived the intended intervention
	2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	N	
	2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	PN	There were two dropouts in the subcutaneous group. One died and one developed local oedema. A proportion of less than 5 % is regarded as small and will not likely affect the outcome
	2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?		
	Risk of bias judgement	**Low risk**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	Vi antar at dataene for om deltakerne fikk bivirkninger eller ikke er rapportert på alle da de skriver: « There were two minor local reactions in the s.c. group (erythema) and one in the i.v. (brusing) group.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?		
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Its likely that they have the same measurement in both groups
	4.3 Were outcome assessors aware of the intervention received by study participants?	NI	Outcome assessors could be blinded for the intervention recived, but there is no information about this.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NI	It is not likely because it is very few cases of adverse effects in both groups.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	N	

	Risk of bias judgement	**Some conserns**	
	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	
Bias in selection of the reported result	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	
	5.3 ... multiple eligible analyses of the data?	NI	
	Risk of bias judgement	**Some conserns**	
Overall bias	**Risk of bias judgement**	**Some conserns**	

Study ID: Slesak 2003, Outcome: Hydration station

Unique ID	Gro Holmelid & Laila Hauge	**Study ID**	Slesak 2003	**Assessor**	
Ref or Label		**Aim**	adhering to intervention (the 'per-protocol' effect)	**The effect of adhering to intervention…**	non-adherence to their assigned intervention by trial participants
Experimental	Subcutaneous fluid hydration	**Comparator**	Intravenous fluid hydration	**Source**	Journal article(s)
Outcome	Hydration status	**Results**		**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	The participants was allocated at the geriatric ward, (Not by computer) after meeting the inclution criteria. The treatment allocation was random by mixing blocks of 6 seald envelopes. 3 contaning i.v. and 3 containing s.c treatment.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	

	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Baseline caracteristisk was simular in both groups
	Risk of bias judgement	**High risk**	Because the participants was allocated at the geriatric ward and not by a computer
Bias due to deviations from intended interventions	2.1 Were participants aware of their assigned intervention during the trial?	Y	The treatment was not binded for any of the groops because of its nature. This was a clinical study that opend up for that the patients could change groups if the patients treatment required that.
	2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?	N	
	2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	NI	It was opened up for the participants to change groups if there were medical or ethical reasons why the participants needed this. Have not found a protocol that supports that this was planned from the beginning. This is not very transparent. The amount of liquid intended in s.c. group appears to be smaller than to i.v. the group. But the reporting is not good enough.
	2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	Y	17 patients switched I.V to s.c and 11 pas switched from s.c. to I.V. No protocol shows that this has been taken into account.
	2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?	PN	They say they have used an ITT only for the two original groups before any switch of intervention. But not everyone has been included in the analysis.
	Risk of bias judgement	**High**	

	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	
Bias due to missing outcome data	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NI	There are a number of analyzes missing for the participants after treatment that have not been explained in the text. Baseline data were not measured on all participants either. Nor is it explained here why they did not measure everyone at baseline.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	PY	
	Risk of bias judgement	**High**	
	4.1 Was the method of measuring the outcome inappropriate?	N	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	
Bias in measurement of the outcome	4.3 Were outcome assessors aware of the intervention received by study participants?	PN	For the outcome measurement, sodium, hematocrit, and creatinine it is likely to assume that the assessors were not aware of the intervention recived by study participants. For the outcome measurement, Mean arterial pressure and puls, the assessors could have been aware of the intervention received by study participants. The study provide no informations of that.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		

	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	We have not found the protocol for this study and the authors do not rapport anything of this in the articel
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	They could also have measured serum osmolality, but they have several different measures that are adequate to say some hydration status
	5.3 ... multiple eligible analyses of the data?	N	
	Risk of bias judgement	**Some conserns**	
Overall bias	**Risk of bias judgement**	**High**	The study is judged to be at high risk of bias in at least one domain for this result.

Study ID: Slesak 2003, Outcome: Adverse effects

Unique ID	Gro Holmelid & Laila Hauge	**Study ID**	Slesak 2003	**Assessor**	
Ref or Label		**Aim**	adhering to intervention (the 'per-protocol' effect)	**The effect of adhering to intervention…**	non-adherence to their assigned intervention by trial participants
Experimental	Subcutaneous fluid hydration	**Comparator**	Intravenous fluid hydration	**Source**	Journal article(s)
Outcome	Adverse effects	**Results**		**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	N	The participants was allocated at the geriatric ward, (Not by computer) after meeting the inclution criteria. The treatment allocation was random by mixing blocks of 6 seald envelopes. 3 contaning i.v. and 3 containing s.c treatment.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	

	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Baseline caracteristisk was simular in both groups
	Risk of bias judgement	**High risk**	Because the participants was allocated at the geriatric ward and not by a computer
Bias due to deviations from intended interventions	2.1 Were participants aware of their assigned intervention during the trial?	Y	The treatment was not binded for any of the groops because of its nature. This was a clinical study that opend up for that the patients could change groups if the patients treatment required that.
	2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2: Were important non-protocol interventions balanced across intervention groups?	N	
	2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	NI	It was opened up for the participants to change groups if there were medical or ethical reasons why the participants needed this. Have not found a protocol that supports that this was planned from the beginning. This is not very transparent. The amount of liquid intended in s.c. group appears to be smaller than to i.v. the group. But this is badly reported
	2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	Y	17 patients switched I.V to s.c and 11 pas switched from s.c. to I.V. No protocol shows that this has been taken into account.
	2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or 2.5: Was an appropriate analysis used to estimate the effect of adhering to the intervention?	PN	They write that they have used an ITT only for the two original groups before any switch of intervention. But then not everyone has been included in the analysis. Table 2 shows the number of reactions, but not the number of patients. It is unclear whether all participants are included in the analysis.

	Risk of bias judgement	**High**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NI	Unclear how many of the participants that have been included in the analyses.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NI	
	Risk of bias judgement	**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Nurses and doctors observed and measured the side effects and wrote them down in a standardized form. Edema that was over 10 cm in diameter was a major side effect. Eczema, thrombophlebitis, and cellulite.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	
	4.3 Were outcome assessors aware of the intervention received by study participants?	NI	We think that it is most likely that the researchers are aware of which group the participants belong to when assessing the outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NI	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	
	Risk of bias judgement	**Some conserns**	
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	We have not found the protocol for this study and the authors do not rapport anything of this in the articel

	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	
	5.3 ... multiple eligible analyses of the data?	N	
	Risk of bias judgement	**Some conserns**	
Overall bias	**Risk of bias judgement**	**High**	The study is judged to be at high risk of bias in at least one domain for this result.

Appendix XI GRADE: Summary of findings tabel

Summary of findings:

Subcutaneous fluid therapy compared to Intravenous fluid therapy for dehydration in the elderly above 65 y

Patient or population: dehydration in the elderly above 65 y
Setting: Nursing homes
Intervention: Subcutaneous fluid therapy
Comparison: Intravenous fluid therapy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Intravenous fluid therapy	Risk with Subcutaneous fluid therapy				
Hydration status (HS) assessed with: Blood sample (Serum osmoality, serum sodium follow up: mean 3 -6 days	-	SMD **0.17 SD higher** (1.34 lower to 1 higher)	-	130 (2 RCTs)	⨁◯◯◯ VERY LOW[a,b]	
Adverse effects	197 per 1 000	**146 per 1 000** (110 to 197)	**RR 0.74** (0.56 to 1.00)	832 (3 RCTs)	⨁⨁◯◯ LOW[c]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **SMD:** Standardised mean difference; **RR:** Risk ratio

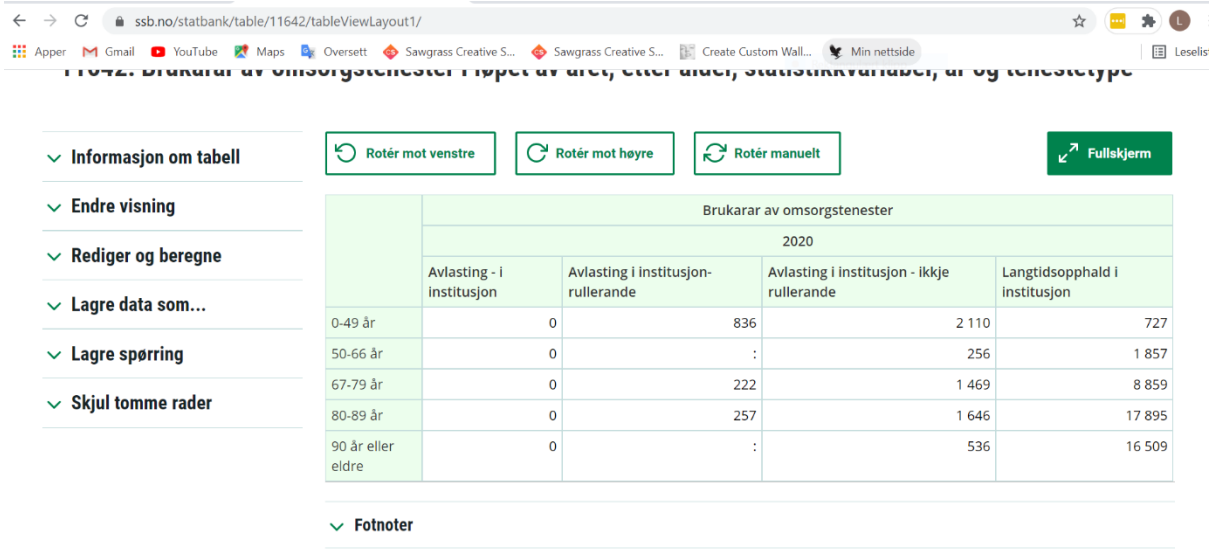
GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is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

Explanations

a. Both studies was judged high risk of bias.
b. The heterogenety was 87%
c. Two studies was judge high and one was judge some conserns.

Appendix XII Documentation from “statistisk sentralbyrå”

Below is an overview of the number of users of care services in Norway in 2020 and their age



	Brukarar av omsorgstenester			
	2020			
	Avlasting - i institusjon	Avlasting i institusjon- rullerande	Avlasting i institusjon - ikkje rullerande	Langtidsopphald i institusjon
0-49 år	0	836	2 110	727
50-66 år	0	:	256	1 857
67-79 år	0	222	1 469	8 859
80-89 år	0	257	1 646	17 895
90 år eller eldre	0	:	536	16 509

Fotnoter

Article

***"Effect and safety of subcutaneous fluid therapy versus intravenous fluid therapy on dehydration in elderly people in nursing homes"*: a systematic review.**

Article draft

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Master in Evidence-Based Practice for Health and Social Sciences

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Number of words: 2686

Abstract

Background

Dehydration in the elderly in nursing homes is a problem that the healthcare- professionals must address daily. It`s already a lot of research on the field, but the systematic review findings are of poor quality. We wanted to investigate the effect of subcutanous fluid therapy in the elderly compared to intravenous fluid therapy, and see if there are any new research that will help enlighten our question.

Methods

A systematic review and meta-analysis were conducted. Systematic search for randomised clinical trials was conducted via the databases of the following platforms: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL and Epistemonikos in April 2020. Two review authors (LH and GH) independently performed study selection, data extraction and risk of bias assessment with the Cochrane Collaborations tools and resources.

Results

A total numer of 5595 studies were found after conducting a literature search. After 740 duplicates were removed, we screened title and abstact of 4855 studies. 26 full-text studies were assessed for eligibility. 22 studies were excluded and in the end, we included 3 randomised controlled trials in this systematic review.

The quality of the included studies was low or had some concerns or high risk of bias. The results indicate a small beneficial effect towards subcutaneous fluid therapy.

Author's conclusions

The result of this review is to weak in order to inform practice, but it doesn´t mean that the effect of the intervention isn´t present, it only means that research have not been able to prove it at this point. The methodological quality of the trials on this topic is of low and very low quality and does not show any effect of the intervention. Based on this we can not recommend to transfer this knowledge into the long time care facilities. Future directions for research should include more qualitative research, and preferably RCT`s, to give high quality research on the topic.

Keywords: Systematic review, meta- analysis, dehydration, fluid therapy, hypodermoclysis, subcutaneous, intravenous.

Background

Dehydration in the elderly in nursing homes is a problem that healthcare- professionals haves to address on a daily basis (Paulis et al., 2018). Due to physiological changes and an increased risk of many diseases the older are more exposed to loss of body water and salt essentials (Thomas et al., 2008; WHO, 2011). The physiological changes with age leads to a reduced homoestatic capacity and makes the elderly population more susceptible to dehydration. The combination of reduced thirst perception and water intake, polypharmacy, cognitive disorders, swallowing malfunction and with kidneys less able to retain water, predispose the elderly to a hydration deficit (Ferry, 2005).

Increased fluid intake and replacement of lost electrolytes are usually sufficient to restore fluid balances in patients with mild or moderate dehydration. For individuals who are mildly dehydrated, just drinking water may be all the treatment that is needed. The oral route is the route of choice for hydration because it is easy to perform and non-invasive, but some circumstances (cognitive disturbances, swallowing changes, low level of consciousness, dementia and agitation), may make it difficult to use this route (Dardaine et al., 1999). When the oral route cannot be instituted, intravenous fluid treatment may be necessary and is most commonly used. But is not always possible to administre, since the peripheral vessels of the elderly undergo physiological changes typical of aging. It may be difficult to access and associated with multiple punctures due to the capillary fragility of the elderly, risk of infection and thrombophlebitis.

To reduce these complications and mainly avoid the numerous attempts of venipuncture, the subcutaneous route has been increasingly used in patients with mild to moderate dehydration.

What is subcutaneous fluid therapy (hyperdermoclysis)?

The subcutaneous route has recently begun to regain recognition as a safe, simple and less-expensive alternative to intravenous fluid hydration in mild to moderately dehydrated patient, particularly in long-term care settings. Hypodermoclysis, also known as subcutanous infusion, is an infusion of isotonic fluids into the subcutaneous tissue. When hydrating the patient

subcutaneously, a thin needle is put into various sites as the abdomen, thighs and arms. Amounts of fluid infused can range between 1000 ml and 2000 ml over a 24-hour period. Normal saline is the crystalloid most often used (Caccialanza et al., 2018). Advantages of hypodermoclysis over IV fluids include ease of administration, minimal medical attendance, and no need for hospitalization for administration. It is particularly useful for the elderly patients in the long time care settings to avoid the danger of admitting patients to hospital. It is also a treatment that is cost-effective.

Methods

A study protocol describing the details of this review was developed in advance and is available in Open Science Framework (Hauge & Holmelid, 2020).

Eligibility criteria

We considered studies for inclusion if they involved elderly above 65 years from the nursing home setting, who were mild to moderate dehydrated. The subcutaneous route was compared with the intravenous route for the administration of fluids. The primary outcomes of interest were objective measures of hydration status, measured in osmolality, urea, mean arterial pressure (MAP) or other methods. Secondary outcome were complications for the two treatment methods, adverse effects. Study designs to be included were randomised controlled trials that met our inclusion criteria.

Databases and litterature search

From the inception to april 2021 we conducted a search in different databases for randomized clinical trials. We searches the databases of the following platforms: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL and Epistemonikos. We also searched the grey literature in Open Grey, PROSPERO and conducted a citation search in Web of Science based on the included studies. The search strategy aimed to find both published and unpublished studies. The reference list of all identified reports and articles were searched for additional studies. We had a restriction for English and Scandinavian language, but not any restrictions relating to date of publishing.

We included different MeSh terms and textwords for dehydration and fluid therapy. These terms can differ between databases and where adapted according to this. The complete search strategy is available in Supplementary appendix 1.

Study selection and quality assessment

Two authors (LH, GH) independently reviewed titles and abstracts, retrieved possibly relevant articles in full-text and assessed them for inclusion in line with the eligibility criteria. We resolved disagreement by discussion and consensus. Two reviewers (LH, GH) independently assessed the risk of bias in the included studies using the RoB2, risk of bias tool. We resolved disagreement by discussion and consensus or by consulting our supervisors.

Data abstraction

Two review authors (LH and GH) independently extracted data from all eligible studies. We discussed and resolved any discrepancies between us via consensus and with our supervisor. We entered data into Review Manager 5 software (RevMan 5) and recorded study details in the Characteristics of included studies and Characteristics of excluded studies, tables 1 and 2.

Data that was relevant to retrieve was: Country of study, number of participants in the intervention and control group, dropout rate, outcome measure and age, gender, effect measure and effect estimate. The data retrieval form was piloted (tested) by two different people.

Data synthesis

We used RevMan 5 software to conduct meta-analysis when at least two RCT-studies provided sufficient numerical data on the same outcome. We illustrated the data by a forest plot.

For continuously measured outcomes, the standardized mean difference between the experimental and control groups was calculated for each study, based on the mean and standard deviation after the treatment, and the number of subjects in the two groups. For the

outcome adverce effects we combined data from all included studies by adding the number of reported adverce effects and the number of infusions.

We used the "Grading of Recommendations, Assessment, Development and Evaluation" (GRADE) approach to rate the overall quality of the evidence for each outcome as high, moderate, low or very low. The software “GRADEpro” was use to rate the result of each outcome and to create a “summary of findings” table.

Results

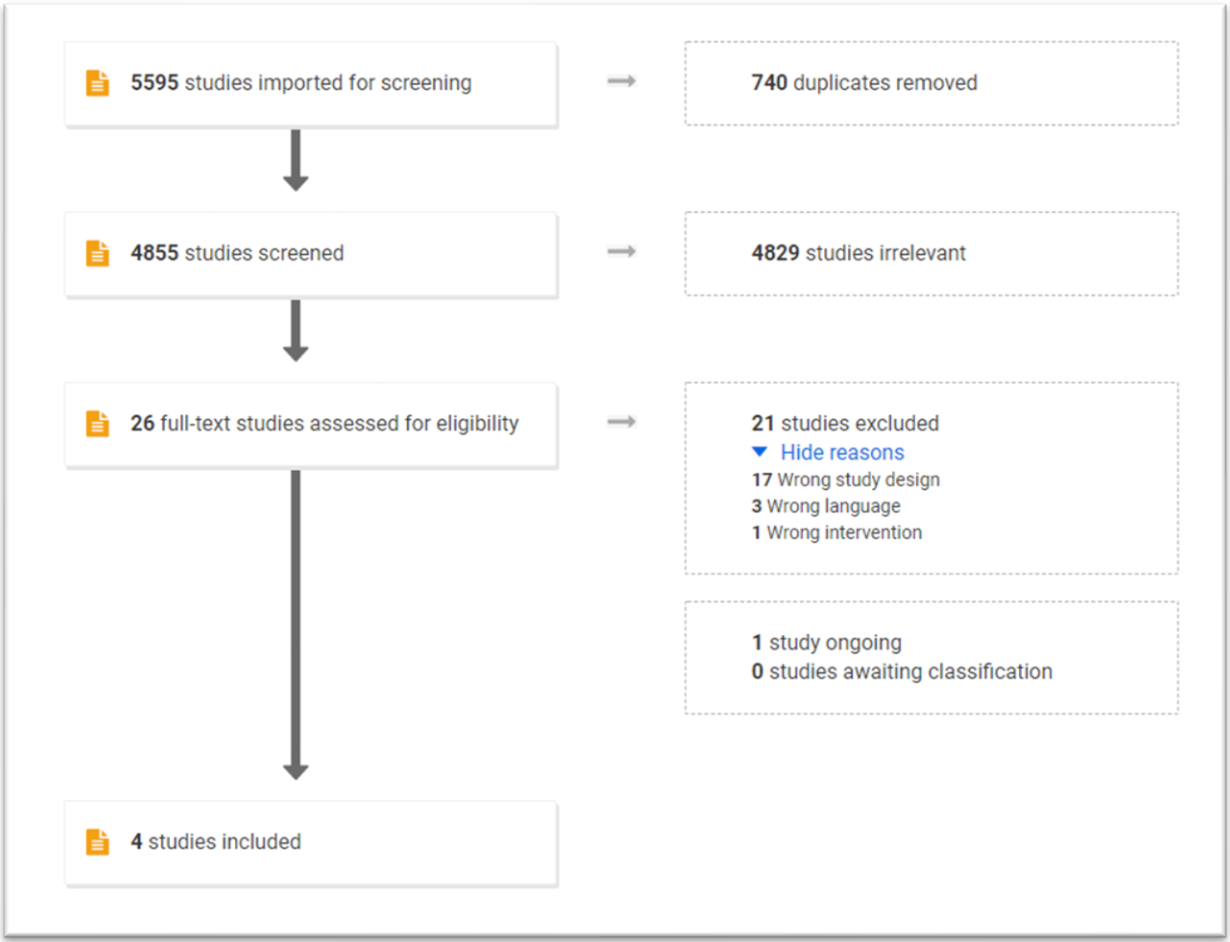
Study selection

A total numer of 5595 studies were found after conducting a literature search. After 740 duplicates were removed, we screened title and abstact of 4855 studies. 26 full-text studies were assessed for eligibility. 22 studies were excluded and the reason for exclusion is presented in appendix VII.

In the end we included 3 RCT‘s that met our inclusion criteria

Figure 1 showes the selection process/flow diagram .

Figure 1



Study characteristics

All of the three randomised controlled trials included participants aged above 65 years. In all studies the mean age is above 80 years, and the study participants are either from nursing home residents or from geriatric wards in the hospital settings.

The participants of these studies were diagnosed with mild to moderate dehydration, and in need of parenteral fluid substitution. All included studies compared intravenous fluid therapy with subcutaneous fluid therapy, where the control group are those who receive intravenous fluid therapy, regardless of fluid type, amount and duration of treatment.

The primary outcome, hydrationstatus, were measured differently across the studies. All three studies rapported adverse effects, our secondary outcome, in number of events, categorized in minor and major adverse effects.

The duration of treatment varied from 48 hours to 6 days, administred in the same way across the three studies. The characteristics of the included studies are summarised in Table 1.

Table 1: Characteristics of the included studies

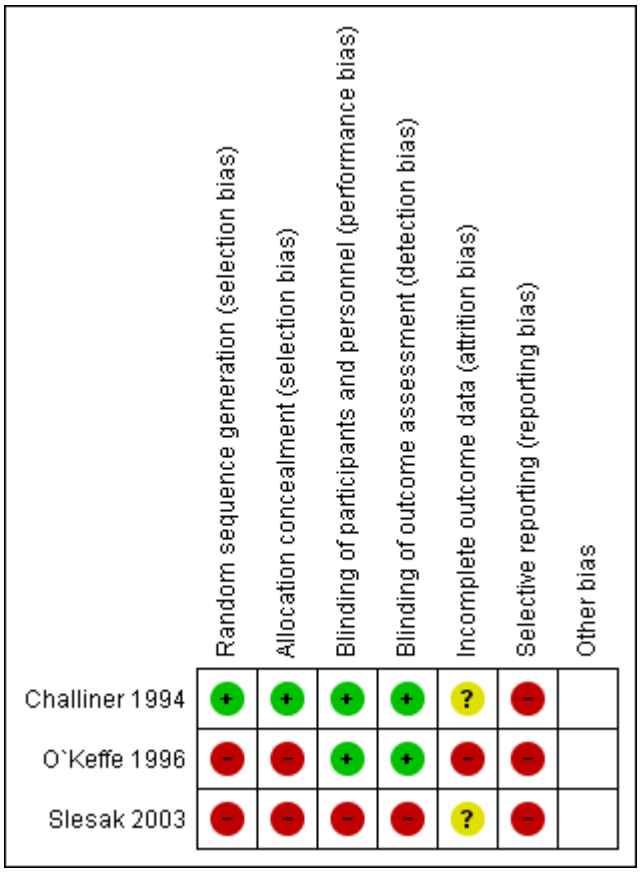
Study, year	Country	Setting	Population	I and C	Outcome	Duration of treatment	Design
(Challiner et al., 1994)	United Kingdom	Hospital setting, elderly care unit	34 acute stroke patients with a mean age of 83,5. Male 23, female 11. Dehydrated.	Intervention: Subcutenous fluid therapy. 2 liters of fluid per 24 h delivered through a butterfly needle. Comparison: Intravenous fluid therapy. 2 liters of fluid per 24 h through an IV access.	Primary oc:Serum osmolalities, mean s-osmolality 296 mOsm/kg at baseline. Secondary oc: Adverce effects. 2 minor erythema in the sc group and 1 bruising in the iv-group.	48 hours	Randomised controlled study

(O'keeffe & Lavan, 1996)	United Kingdom	Hospital setting, acute geriatric unit	60 geriatric patients with cognitive impairment. With a mean age of 82,5. Male 23, female 37 Mild dehydration or poor oral intake.	Intervention: SC fluid therapy. Up to 2 liters of fluid per 24 h with butterfly needle. Comparison: Intravenous fluid therapy through IV access, up to 2 liters fluid per 24 hours	Primary outcome: , Serum creatinin, mean 109,5 umol/l at baseline Secondary oc: Adverce effects. 2 local oedema in sc group and 0 in iv group.	48 hours	Randomised controlled study
(Slesak et al., 2003)	Germany (written in english)	Hospital setting, Geriatric ward in the Geriatric department	96 geriatric patients, mean age 85,3. Male 29, female 67. Mild to moderate dehydrated	Intervention: Subcutanous fluid therapy, up to 1,5 liters fluid per 24 h.Comparison: Intravenous fluid therapy, up to 1,5 liters per 24 hours.	Primary outcome: Sodium, mean 137 mmol/l at baseline. Secondary oc: Adverce effects.	6 days	Randomised controlled study

Risk of bias and overall quality

Using GRADE, the overall quality of the evidence for all outcomes were judged to be low or very low. The Cochrane risk of bias tool, RoB 2.0 (Lefebvre et al., 2011), were be used to assess the risk of bias in randomised controlled trials.

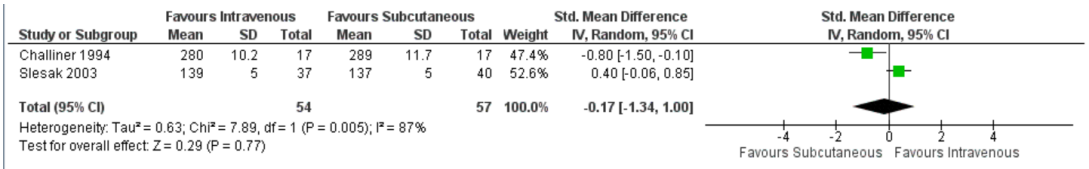
Details on our risk of bias and GRADE assessment are available in the Appendix X and XI.



Effect of the intervention

Hydration status

We have analyzed the available data for the included studies in two meta-analyzes using Revman 5 software, cf. section 4.6. For the outcome measure, hydration status, the studies Challiner and Slesak reported data with different measurement methods for the same outcome. Due to the different scales used to report hydration status as a continuous outcome, these results are reported as standardized mean differences (SMD) cf. point 4.6. From Challiner, we extracted the blood value, osmolality, and compared this with the blood value, sodium, from Slesak after the fluid treatment in the two groups. The result of this analysis is shown in the figure below.



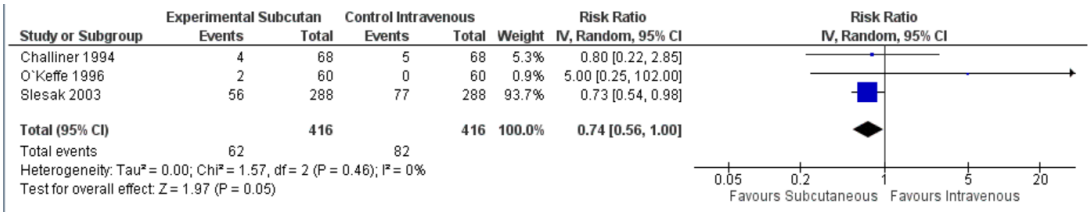
Caption

Forest plot of comparison: 4 Subcutaneous fluid treatment versus Intravenous fluid treatment, outcome: 4.1 Hydration status (Blodsample; Serum sodium and serum osmolality).

The measure of effect from this analysis shows an SMD of 0.17, which means that subcutaneous fluid therapy is favored compared to intravenous fluid therapy. The 95% confidence interval shows -1.34-1.00. Our analysis comes out with a very large heterogeneity (cf. section 4.7.2) of 87% and a p-value of 0.005 which means that there is a high degree of variation between the studies which is not random and which should be explained. Reasons why they are different can be explained by the fact that the hydration status has been measured in different ways in the two studies and that we have too few studies in our analysis for us to get an effect estimate with a lower heterogeneity.

Adverse effect

If we look at our second outcome measure, adverse effects, we had to make an analysis of how many side effects had been reported in the different groups against the number of fluid infusion treatments. For this analysis, we were able to include all studies as they had data on adverse effects. The result of the meta-analysis on this outcome measure is shown below.



Caption

Forest plot of comparison: Outcome: Adverse effects.

The number of events indicates how many side effects the participants experienced after x number of infusions in subcutaneous group versus intravenous group.

This analysis shows a relative risk (RR) of 0.74, with a 95% confidence interval of 0.56-1.00 favoring the subcutaneous group. The heterogeneity becomes 0% with a p-value of 0.05. This is probably related to the fact that there is one of the studies dominates in this analysis and which is weighted 93.7%. And then it means less that the studies of O`Keeffe and Challiner have broad confidence intervals because it does not affect the result to the same degree as in

the analysis above. Overall, we see from the analysis that there is a 26% lower risk of adverce effects with subcutaneous fluid therapy than with intravenous fluid therapy, but we can not conclude that this effect is significant, as we have very few studies in our analysis and there is an uncertainty in whether all studies have had different ways of registering these side effects. There is no information on how this has taken place in O`Keeffe and Challinger, while in Slesak it was nurses and doctors who observed and measured the side effects and wrote them down in a standardized form.

Discussion

Summary of evidence

Methodological challenges and unclear reporting were a significant challenge in the included studies. Due to insufficient information in the studies and then primarily in the studies of O`Keeffe (1996) and Challiner (1994), we could not make a meta-analysis for all the data and therefore had to make a post hoc analysis for our secondary outcome measure. This was not predetermined in our protocol. The reason for that choice was that the studies did not report a mean and a standard deviation (SD), as for the outcome hydration status. The data available to us were only the number of events of the outcome and number of fluid infusions.

We had to take into account errors that could effect the result, for example if participants contributed to multiple measurement in the same analysis (unit of analysis errors) In Slesak (2003) there are more events than participants, so we can assume that this is the case. In addition, it is badly reported to the reader on how to interpret the numbers.

We also had challenges in extracting measurement data from the study of Slesak on the outcome measure, hydration status, because of the different measures on the outcome. Furthermore, it was reported in Slesak that the participants were allowed to change group if there were medical- or ethical reasons for a switch between interventions. But it gave us some challenges to be able to understand who had switched interventions and at what time of the process, because of poor reporting in the studies.

GRADE helped us to support our judgement about the degree of confidence in the results of the studies in our systematic review. Our two outcome measures, hydrating status and adverce effects, were judged differently.

For the outcome measure hydration status, we judged to have a very low confidence in this result. The true effect can most likely be different from what we got from our analysis, cf. section 5.5. Based on this, our findings for this outcome measure are not generalizable to the population. For outcome measures, adverse effects, we came out with a low GRADE assessment, which means that our confidence in this effect estimate is limited. And the true result will probably be different than what we got in our analysis. We can therefore not generalize this result to the population.

Summary of findings:

Subcutaneous fluid therapy compared to Intravenous fluid therapy for dehydration in the elderly above 65 y

Patient or population: dehydration in the elderly above 65 y
Setting: Nursing homes
Intervention: Subcutaneous fluid therapy
Comparison: Intravenous fluid therapy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Intravenous fluid therapy	**Risk with Subcutaneous fluid therapy**				
Hydration status (HS) assessed with: Blood sample (Serum osmoality, serum sodium follow up: mean 3 -6 days	-	SMD **0.17 SD higher** (1.34 lower to 1 higher)	-	130 (2 RCTs)	⨁◯◯◯ VERY LOW [a,b]	
Adverse effects	197 per 1 000	**146 per 1 000** (110 to 197)	**RR 0.74** (0.56 to 1.00)	832 (3 RCTs)	⨁⨁◯◯ LOW [c]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **SMD:** Standardised mean difference; **RR:** Risk ratio

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

Explanations

a. Both studies was judged high risk of bias.
b. The heterogenety was 87%
c. Two studies was judge high and one was judge some conserns.

Comparison with existing resarch on the field and implication for further research

When we searched for knowledge on our research question, we found 6 systematic reviews that we critically evaluated after ROBIS (Whiting et al., 2016). We judged them all to have high risk of bias and because of this we had low confidence in the results. Some of the included studies in these reviews were out of date or didn`t answer our research question. Very few RCT were included in these reviews. Based on this, there was still a need to conduct

our systematic review in the hope of finding more recent RCT studies that could provide us with answers to our question

Conclusion

The result of this review is to weak in order to inform practice, but it doesn´t mean that the effect of the intervention isn´t present, it only means that research havent been able to prove it yet. The methodological quality of the trials on this topic is of low and very low quality and it is does not show any effect of the intervention. Based on this we can not recommend to transfer this knowledge in to the long time care facilities. Future directions for research should include more qualitative research, and preferably RCT`s, to give high quality research on the topic.

Acknowledgments

Many thanks to all our fellow students and in particular to Eva Marie-Louise Denison and Hans Lund, our supervisors. Through their extensive professional knowledge, safe guidance and optimistic feedback, they have always given us the belief that it has been possible to get through with the project.

Supplementary appendix 1

Search in Cochrane Library

```
Search Name:    Masteroppgave i KBP Søkedato 290820
Date Run:       13/12/2020 17:44:39
Comment:

ID      Search  Hits
#1      MeSH descriptor: [Water Loss, Insensible] explode all trees     285
#2      MeSH descriptor: [Water-Electrolyte Imbalance] explode all trees
1694
#3      (dehydrat*):ti,ab,kw OR (water NEXT stress):ti,ab,kw (Word variations
have been searched)     3283
#4      (Water NEXT Electrolyte NEXT Imbalance):ti,ab,kw OR (Insensible NEXT
Water NEXT Loss):ti,ab,kw OR (Fluid NEXT Elektrolyte NEXT Imbalance):ti,ab,kw OR
(Drying NEXT (up OR out)):ti,ab,kw OR (Fluid NEXT deprivation*):ti,ab,kw
181
#5      (deprivation* NEXT of NEXT water):ti,ab,kw OR (Fluid NEXT loss):ti,ab,kw
OR (Loss NEXT of NEXT body NEXT water):ti,ab,kw OR (Decrease NEXT in NEXT total
NEXT body NEXT fluid):ti,ab,kw OR (Reduction NEXT of NEXT water NEXT
content):ti,ab,kw       181
#6      (exsoccation*):ti,ab,kw OR (cellular NEXT desiccation*):ti,ab,kw OR
(anhydration*):ti,ab,kw OR (hypodration*):ti,ab,kw OR (enhydration*):ti,ab,kw
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5
#8      (inappropriate NEXT ADH NEXT syndrome):ti,ab,kw OR (refeeding NEXT
syndrome):ti,ab,kw OR (water NEXT intoxication):ti,ab,kw        95
#9      #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8    4908
#10     MeSH descriptor: [Hypodermoclysis] explode all trees    15
#11     (hypodermoclys*):ti,ab,kw OR (infusion*):ti,ab,kw OR (subcutaneous NEXT
(fluid or hydration*)):ti,ab,kw (Word variations have been searched)    67796
#12     MeSH descriptor: [Fluid Therapy] explode all trees      1684
#13     MeSH descriptor: [Infusions, Subcutaneous] explode all trees    153
#14     MeSH descriptor: [Infusions, Parenteral] explode all trees      12410
#15     MeSH descriptor: [Infusions, Intravenous] explode all trees     10270
#16     MeSH descriptor: [Administration, Intravenous] explode all trees
18586
#17     MeSH descriptor: [Rehydration Solutions] explode all trees      293
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#24     randomized NEXT controlled NEXT trial   867075
#25     RCT     34400
#26     #24 OR # 25     955952
#27     #23 AND #26     1221
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Search in MEDLINE

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to 24 nov, 2020>

Search Strategy:

---

1 exp Dehydration/ (13655)

2 exp Water-Electrolyte Imbalance/ (62913)

3 exp Water Loss, Insensible/ (2393)

4 dehydrat*.tw. (44632)

5 Water-Electrolyte Imbalance.tw. (113)

6 water loss insensible.tw. (0)

7 water stress.tw. (4558)

8 drying up.tw. (157)

9 drying out.tw. (181)

10 fluid deprivation.tw. (205)

11 fluid loss.tw. (1333)

12 loss of body water.tw. (86)

13 decrease in total body fluid.tw. (2)

14 reduction of water content.tw. (64)

15 exiccation.tw. (0)

16 cellular desiccation.tw. (10)

17 anhydration.tw. (6)

18 hypodration.tw. (0)

19 enhydration.tw. (0)

20 volunary dehydration.tw. (0)

21 hypercalcemia.tw. (13588)

22 hypercalcciuria.tw. (0)

23 hyperkalemia.tw. (6194)

24 hypermagnesemia.tw. (510)

25 hyperphosphatemia.tw. (3475)

26 hypophosphatemia.tw. (3777)

27 inappropriate ADH syndrome.tw. (27)

28 refeeding syndrome.tw. (452)

29 water intoxication.tw. (887)

30 or/1-29 (123381)

31 exp Fluid Therapy/ (20843)

32 exp Infusions, Subcutaneous/ (1255)

33 exp Infusions, Parenteral/ (93428)

34 exp Infusions, Intravenous/ (55692)

35 exp Administration, Intravenous/ (145302)

36 exp Hypodermoclysis/ (135)

37 exp Rehydration Solutions/ (1473)

38 fluid therapy.tw. (3607)

39 hypodermoclysis.tw. (133)

40 infusion fluid.tw. (281)

41 infusion liquid.tw. (29)

42 intravenous fluid.tw. (2843)

43 fluid resuscitation.tw. (5343)

44 fluid therap*.tw. (3639)

45 rehydration*.tw. (8403)

46 infusion* intravenous.tw. (182)

47 infusion* parenteral.tw. (7)

48 infusion* subcutaneous.tw. (21)

49 hypodermoclys*.tw. (134)

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51 administration subcutaneous.tw. (105)

52 or/31-51 (212581)

53 exp Randomized Controlled Trial/ (532139)

54 ((random* and (controlled or control or placebo or versus or vs or group or groups or comparison or compared or arm or arms or crossover or cross-over) and (trial or study)) or ((single or double or triple) and (masked or blind*))).tw. (788815)

55 53 or 54 (952172)

56 30 and 52 and 55 (798)

****

Search in EMBASE

EMBASE søk 10 oktober 2020

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2	dehydration/	13409	Advanced	More
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4	fluid-electrolyte imbalance.tw.	23	Advanced	More
5	water loss insensible.tw.	0	Advanced	More
6	water stress.tw.	4371	Advanced	More
7	drying up.tw.	153	Advanced	More
8	drying out.tw.	175	Advanced	More
9	fluid deprivation.tw.	204	Advanced	More
10	fluid loss.tw.	1304	Advanced	More
11	loss of body water.tw.	84	Advanced	More
12	decrease in total body fluid.tw.	2	Advanced	More
13	reduction of water content.tw.	60	Advanced	More
14	exiccation.tw.	0	Advanced	More
15	cellular desiccation.tw.	10	Advanced	More
16	anhydration.tw.	6	Advanced	More
17	hypodration.tw.	0	Advanced	More
18	enhydration.tw.	0	Advanced	

				More
	19	volunary dehydration.tw.	0	Advanced
				More
	20	hypercalcemia.tw.	13393	Advanced
				More
	21	hypercalcciuria.tw.	0	Advanced
				More
	22	hyperkalemia.tw.	6022	Advanced
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	23	hypermagnesemia.tw.	496	Advanced
				More
	24	hyperphosphatemia.tw.	3378	Advanced
				More
	25	hypophosphatemia.tw.	3676	Advanced
				More
	26	inappropriate ADH syndrome.tw.	27	Advanced
				More
	27	refeeding syndrome.tw.	431	Advanced
				More
	28	water intoxication.tw.	883	Advanced
				More
	29	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28	81683	Advanced
				More
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				More
	31	hypodermoclysis/	129	Advanced
				More
	32	infusion fluid/	0	Advanced
				More
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				More
	34	hypodermoclysis.tw.	131	Advanced
				More
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				More

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☐	46	administration subcutaneous.tw.	102	Advanced More
☐	47	30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	33155	Advanced More
☐	48	29 and 47	5410	Advanced More

Search in Epistemonikos

Epistimonikos søkestrategi, masteroppgave i KBP, 22 nov 2020

(title:(dehydrat*) OR abstract:(dehydrat*)) OR (title:(water stress) OR abstract:(water stress)) OR (title:(water electrolyte imbalance) OR abstract:(water electrolyte imbalance)) OR (title:(water loss insensible) OR abstract:(water loss insensible)) OR (title:(fluid electrolyte imbalance) OR abstract:(fluid electrolyte imbalance)) OR (title:(drying (up OR out)) OR abstract:(drying (up OR out))) OR (title:(fluid deprivation*) OR abstract:(fluid deprivation*)) OR (title:(deprivation* water) OR abstract:(deprivation* water)) OR (title:(fluid loss) OR abstract:(fluid loss)) OR (title:(loss of body water) OR abstract:(loss of body water)) OR (title:(decrease in total body fluid) OR abstract:(decrease in total body fluid)) OR (title:(reduction of water content) OR abstract:(reduction of water content)) OR (title:(hyper (calcemia OR calcciuria OR kalemia OR magnesemia OR natremia OR phosphatemia)) OR abstract:(hyper (calcemia OR calcciuria OR kalemia OR magnesemia OR natremia OR phosphatemia))) OR (title:(inappropriate ADH syndrome) OR abstract:(inappropriate ADH syndrome)) OR (title:(refeeding syndrome) OR abstract:(refeeding syndrome)) OR (title:(water intoxication) OR abstract:(water intoxication)) AND (title:(hypodermoclys*) OR abstract:(hypodermoclys*)) OR (title:(subcutaneous (fluid OR hydration*)) OR abstract:(subcutaneous (fluid OR hydration*))) OR (title:(Fluid therap*) OR abstract:(Fluid therap*)) OR (title:(infusions (subcutanious OR parenteral OR intravenous)) OR abstract:(infusions (subcutanious OR parenteral OR intravenous))) OR (title:(administration (intravenous OR subcutaneous)) OR abstract:(administration (intravenous OR subcutaneous))) OR (title:(rehydration solution*) OR abstract:(rehydration solution*)) OR (title:(hypodermoclys*) OR abstract:(hypodermoclys*)) OR (title:(infusion*) OR abstract:(infusion*)) OR (title:(fluid resurcitation*) OR abstract:(fluid resurcitation*)) OR (title:(subcutaneous hydration*) OR abstract:(subcutaneous hydration*)) OR (title:(rehydrat*) OR abstract:(rehydrat*)) OR (title:(intravenous) OR abstract:(intravenous))

Treff: 14

Fikk ikke noen treff på følgende ord: (Er derfor blitt utelatt i søkestrategi)

- Exsoccation
- Cellular desiccation
- Anhydration
- Enhydration
- hypodration

Search in CINAHL

EBSCOhost

Monday, November 16, 2020 1:06:42 PM

#	Query	Limiters/Expanders	Last Run Via	Results
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S22	S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	26,050
S21	AB administration intravenous OR AB administration subcutaneous fluid	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	2,009
S20	AB infusions parenteral OR AB infusions subcutaneous OR AB hypodermoclys*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	358
S19	AB fluid resuscutation OR AB rehydrat* OR AB infusions intravenous	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	3,845
S18	AB fluid therap* OR AB Intravenous therap* OR AB Fluid intake output-measur*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	1,516
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S16	(MH "Intravenous Therapy+")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases Search Screen - Advanced	12,667

		Search modes - Boolean/Phrase	Search Database - CINAHL	
S15	(MH "Fluid Therapy+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	19,402
S14	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	20,675
S13	AB water intoxication	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	63
S12	AB hypophosphatemia OR AB inappropriate ADH syndrome OR AB refeeding syndrome	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	711
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S7	AB exsiccation OR AB cellular desiccation OR	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases	0

	AB anhydration	Search modes - Boolean/Phrase	Search Screen - Advanced Search Database - CINAHL	
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S5	AB fluid deprivation OR AB Deprivation of water OR AB fluid loss	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	406
S4	AB water stress OR AB drying up OR AB drying out	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	50
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S1	(MH "Fluid-Electrolyte Imbalance+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL	15,326

Referanser

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