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SUMMARY WITH CRITICAL APPRAISAL

Hypodermoclysis for Frail Patients and Patients in Long Term Care: A Review of Clinical Effectiveness, Cost Effectiveness, and Guidelines

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Abbreviations

HDC	hypodermoclysis
IV	intravenously
RCT	randomized controlled trial
SR	systematic review

Context and Policy Issues

Hypodermoclysis (HDC) is a method of administering fluids or medication subcutaneously (under the skin), as opposed to intravenously (IV; into a vein) or intramuscularly (into a muscle). It is a viable option for many medications and fluids, especially if the individual is unable to take oral medication or if the individual has unsuitable veins for IV fluids.[1] Benefits of subcutaneous administration of medication include lower pain (as there are fewer pain receptors), good irrigation, and lower proteolytic activity. However, the bioavailability of substances administered in this method is uncertain. In mild to moderate dehydration, HDC of fluids is a relatively accepted form of rehydration therapy, especially when other routes are inaccessible or ineffective.[1] However, HDC can be a costly procedure, and its effectiveness is debated, with a lack of literature or evidence for effectiveness, especially in specific populations.[1-3] Therefore, the purpose of this report is to examine the clinical and cost effectiveness of HDC in frail patients or patients residing in long term care, as well as evidence-based guidelines regarding the use of HDC in these patients.

This report is an upgrade of a previous 2020 CADTH report titled “Hypodermoclysis for Frail Patients and Patients in Long Term Care: Clinical Effectiveness, Cost Effectiveness, and Guidelines”,[4] therefore it summarizes and critically appraises the articles identified in that report.

Research Questions

1. What is the clinical effectiveness of hypodermoclysis in frail patients who are at risk of dehydration or who are dehydrated in any setting?
2. What is the clinical effectiveness of hypodermoclysis in geriatric patients who are at risk of dehydration or who are dehydrated in long term care?
3. What is the cost-effectiveness of hypodermoclysis in frail patients who are at risk of dehydration or who are dehydrated in any setting?
4. What is the cost-effectiveness of hypodermoclysis in geriatric patients who are at risk of dehydration or who are dehydrated in long term care?
5. What are the evidence-based guidelines regarding the use of hypodermoclysis in frail patients or patients in long term care?

Key Findings

Two systematic reviews and one randomized controlled trial were identified regarding hypodermoclysis in patients who are frail or who are in long term care. Hypodermoclysis appeared to have fewer adverse effects or complications when compared with intravenous fluids but did not have a significantly better clinical improvement of dehydration. The studies were of low quality, with poor reporting of methods and small sample sizes. No economic

evaluations were identified regarding hypodermoclysis in frail patients or patients in long term care, and no evidence-based guidelines were identified.

Methods

Literature Search Methods

This report makes use of a literature search developed for a previous CADTH report.[4] For the previous report, a limited literature search was conducted by an information specialist on key resources including Ovid MEDLINE, Ovid EMBASE, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were hypodermoclysis. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 01, 2015 and June 29, 2020.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Q1,3,5: Patients in any setting (e.g. acute, long term care, or palliative care) who are frail (as noted by the authors or according to a frailty scale or index) who are at risk of or who are dehydrated Q2,4-5: Geriatric patients (i.e., age 65 and older) receiving long term care who are at risk of or who are dehydrated
Intervention	Hypodermoclysis (i.e., subcutaneous infusion of fluids, interstitial infusion)
Comparator	Intravenous infusion, oral rehydration, no hypodermoclysis (usual care or a control group)
Outcomes	Q1: Clinical effectiveness (e.g., change in hydration, quality of life and comfort, safety [e.g., adverse events], change in delirium) Q2: Cost effectiveness (e.g., quality adjusted life years, incremental cost effectiveness ratios) Q3: Recommendations regarding the use of hypodermoclysis in long term care, the use of hypodermoclysis in frail patients, the recommended location for the subcutaneous line for hypodermoclysis injection, or the recommended infusion method (e.g. gravity, pump) for hypodermoclysis
Study Designs	Systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2015. Articles were excluded if they were not clear on the population being examined or were mixed populations with no indication of how many individuals fit the inclusion criteria of this report. Articles were also excluded if the patients were not in long term care (e.g., acute care or palliative care) and were not specified as being frail. Systematic reviews (SRs) in which all relevant studies were captured in other more recent or more comprehensive SRs were excluded. Primary

studies retrieved by the search were excluded if they were captured in one or more included SRs. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included publications were critically appraised by one reviewer using the following tools as a guide: A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR 2)[5] for SRs and the Downs and Black checklist[6] for randomized controlled trials (RCTs). Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 65 citations were identified in the literature search. Following screening of titles and abstracts, 62 citations were excluded and three potentially relevant reports from the electronic search were retrieved for full-text review. No potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially relevant articles, no publications were excluded, and three publications met the inclusion criteria and were included in this report. These comprised two systematic reviews and one randomized controlled trial. Appendix 1 presents the PRISMA[7] flowchart of the study selection.

Additional references of potential interest are provided in Appendix 6.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

Two SRs were identified with relevance to the research question and inclusion criteria of this report. Forbat et al[2] was published in 2016, including all relevant studies and systematic reviews prior to September 2015. Forbat et al[2] included English language studies but were not specific in what study designs were eligible for inclusion. Duems-Noriega and Ariño-Blasco[1] was published in 2015, and included “original articles”, reviews, letters to the editor, or communications with no limitation on date published or language, but did not specify what date the search was performed.

The SRs had broader inclusion criteria than this report. Forbat et al[2] included studies examining the mechanisms of delivery, the location of HDC, the type of fluids, and the quantity of fluids in patients with advanced illness, which included patients in acute settings and palliative care. Duems-Noriega and Ariño-Blasco included administration of medication subcutaneously as well as fluid administration.[1] Only the studies examining relevant population groups and interventions were extracted from these SRs.

There was overlap of one relevant study between the two SRs. The degree of overlap is illustrated in tabular form in Appendix 5.

The included primary study was an RCT with a crossover design, in which the patients received both the intervention and the control, thereby acting as their own controls.[8]

Country of Origin

The first author of Forbat et al is from Australia.[2] The first author for Duems-Noriega and Ariño-Blasco is from Spain.[1]

The RCT was conducted in Turkey.[8]

Patient Population

Forbat et al[2] included studies examining adults over 18 with advanced illnesses who were receiving subcutaneous hydration, which included patients in a residential facility or aged-care facility (i.e., long term care). Duems-Noriega and Ariño-Blasco[1] included studies with patients in long term care and frail elderly patients, but were not clear in what was the overall eligible population was for the SR. The number of relevant participants from Forbat et al[2] was 55 for one of the included primary studies, and not reported for the other. In Duems-Noriega and Ariño-Blasco,[1] the primary studies included 148 participants.

The population for the RCT (n = 30) was geriatric patients over the age of 65 living in a long term private care facility.[8] The majority of patients were female.[8]

Interventions and Comparators

The relevant interventions in the SRs was HDC.[1,2] The eligible comparator for Forbat et al[2] was fluid administered through an IV line. The comparator was not specified for Duems-Noriega and Ariño-Blasco,[1] but was assumed to be potentially all comparators as the search strategy was broad.

The intervention for the included RCT (Esmeray et al) was three consecutive HDC infusions. The infusions were 1000mL of 0.9% saline solution administrated with a 21- to 23-gauge subcutaneous butterfly needle at a rate of 125mL per hour. HDC was compared to three consecutive IV infusions, but the rate of infusion and the amount of fluid infused was not reported.[8]

Outcomes

The outcomes eligible for Forbat et al were complications associated with hydrodermoclysis.[2] The outcomes for Duems-Noriega and Ariño-Blasco[1] were not specified in the methods, but the included primary studies had measured outcomes of urea levels, sodium levels, and creatinine levels, discomfort, feasibility, osmolarity, and function.

The outcomes for Esmeray et al[8] were complications or adverse events, the use of consumables, urine density, pH values of urine, and vital signs, but only complications, number of catheters used, duration of catheter use, and time to insert catheter were reported in the results.

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3

One SR was of moderate quality.[2] One SR was of very-low quality,[1] as the methodology used to create the SR was unclear.

Forbat et al[2] had a clear aim and research question. It also was registered in PROSPERO (a prospective registrar for systematic reviews) prior to the report being completed, showing

a priori methods. The SR also did a preliminary search (i.e., scoping search) to determine appropriate inclusion and exclusion criteria for the review.[2] The search included multiple databases, and two reviewers both independently selected studies and extracted data.[2] However, the review was missing some outcome information, including clinical and functional outcomes that were available in the original primary study abstract, but not reported in the SR. It was unclear why these outcomes were not included, and it was unclear if some results were not included due to selective publishing of results.[2]

Duems-Noriega and Ariño-Blasco were unclear regarding their methodology.[1] The inclusion and exclusion criteria and eligible population groups were unclear, and there was no protocol or a priori methodology provided. There was additionally no information on study selection or data extraction, so it is unknown if bias was introduced in this stage.[1] The authors also do not provide an appropriate count of how many studies were identified in the initial search, and how many studies were excluded, therefore making it difficult to determine whether the search yielded an expected number of results for their parameters.[1] It is also unclear when the search was performed, so, although assumed to be before 2015 (the publication date of the SR), it is not clear how long prior to publication the search was performed.[1] Additionally, details from the results of the studies are missing, such as ages of the patients, ratios of the genders, rates of infusion, and the type of infusion.[1]

The methodology of the included RCT was poorly reported, therefore its quality is unclear.[8] The aim of the study was clear, but the control group was not sufficiently detailed and was not defined adequately.[8] It was unclear how much time occurred between infusions and how much time occurred between the intervention and control group (or control and intervention group).[8] The randomization technique used is not described, therefore it is not possible to judge whether the randomization was adequate or maintained.[8] The authors of the study also reported what outcomes were to be collected, but did not report what methods were used to collect the data, such as what scales were used, what threshold was used to determine what counted as an adverse event, or why some outcomes were included over others.[8] Additionally, the authors did not report on all the outcomes mentioned in the methods, namely, urine density, urine pH levels, and patient vital signs. It was not clear why these results were not included.[8] Finally, the sample size was relatively small (n = 30), and there was no power calculation performed to determine if the study was appropriately powered to find a significant difference.

Summary of Findings

Appendix 4 presents the main study findings and authors' conclusions.

Clinical Effectiveness of Hypodermoclysis

What is the clinical effectiveness of hypodermoclysis in frail patients who are at risk of dehydration or who are dehydrated in any setting?

The primary studies included in the SRs were from 2004 or earlier.[1,2]

One primary study included in Forbat et al[2] was a prospective observational study, where frail elderly adults (n = 55) were given HDC at a rate of 20 to 75 mL/h daily, and had fewer fluid-related complications when compared with individuals given IV fluids for dehydration (P = 0.04).[2] This prospective study was also included in Duems-Noriega and Ariño-Blasco.[1] Duems-Noriega and Ariño-Blasco reported that general or clinical improvement was not statistically different between the groups (P = 0.19), and local reactions were lower in the group receiving HDC.[1]

Duems-Noriega and Ariño-Blasco[1] included one uncontrolled study examining outcomes before and after HDC administration in frail patients. The uncontrolled study examined 57 frail, elderly patients, 77% of which had clinical improvement after HDC (P value not reported).

What is the clinical effectiveness of hypodermoclysis in geriatric patients who are at risk of dehydration or who are dehydrated in long term care?

One primary study identified in Forbat et al[2] was an SR which concluded that HDC was safe and effective for older people in long term care with mild to moderate dehydration, but no numerical or statistical results were provided, and it was unclear what HDC was compared to.

One uncontrolled study with 36 patients in a care home found no improvements in serum sodium, urea, or creatinine levels (P values not reported).[1] 71% of these patients returned to a clinical baseline.[1]

In the included RCT (N = 30), HDC had fewer complications overall when compared with IV infusion (P = 0.001). Patients had significantly less redness after the first administration of fluid, and the number of patients with agitation and bleeding was fewer after all administrations with HDC compared with IV (P = 0.001 for all).[8] The number of catheters used was higher in patients receiving IV fluids and the insertion time was longer when compared with HDC (P = 0.001 for both). However, catheter duration was longer in patients when they received HDC compared with IV (P = 0.001).[8]

Cost-Effectiveness of Hypodermoclysis

What is the cost-effectiveness of hypodermoclysis in geriatric patients who are at risk of dehydration or who are dehydrated in long term care?

No relevant cost effectiveness evidence regarding the HDC for patients in long term care settings was identified; therefore, no summary can be provided.

What is the cost-effectiveness of hypodermoclysis in frail patients who are at risk of dehydration or who are dehydrated in any setting?

No relevant cost effectiveness evidence regarding the HDC for frail patients was identified; therefore, no summary can be provided.

Guidelines

What are the evidence-based guidelines regarding the use of hypodermoclysis in frail patients or patients in long term care?

No evidence-based guidelines were identified regarding HDC for frail patients or patients in long term care settings; therefore, no summary can be provided.

Limitations

The articles included within this report were relatively outdated – despite the SRs being published in 2015[1] and 2016[2] respectively, the articles identified by those reviews were from 2000 and earlier. While studies that are outdated can still provide valuable information, the care provided in those studies and the techniques and equipment used may not reflect current care. Additionally, there were few studies examining HDC in frail patients or in long term care settings. This scarcity of evidence and well conducted studies with many patients in a variety of settings makes decision making difficult, as small studies conducted in

specific setting may not be generalizable to all settings or to the Canadian context. The evidence base was limited, and of low quality, as the studies identified may have a high risk of bias. This also limits conclusions that can be drawn from the studies.

Finally, there were no cost studies identified in the literature. This precludes any conclusions that can be made regarding the cost of treatment, and whether any potential clinical effectiveness also translates into cost-related effectiveness for HDC. There were also no evidence-based guidelines identified.

Conclusions and Implications for Decision or Policy Making

Two SRs[1,2] and one RCT[8] were identified regarding the clinical effectiveness of HDC in patients who are frail or who are staying in long term care. Overall, based on low-quality evidence, HDC showed fewer complications than IV administered fluids. One SR reported on clinical improvement and did not find a statistically significant difference between HDC and IV fluids. There were no economic evaluations or evidence-based guidelines identified in the literature.

The methodology of the two SRs by Forbat et al and Duems-Noriega et al were moderate quality[2] and very low quality[1] respectively. Methodological and reporting issues with the SRs included missing methodology, outcomes, and results, and unclear data extraction or selection methods. The searches were generally broad and conducted in multiple databases.

The RCT was of low quality.[8] It was unclear what the randomization method was, the interventions were unclear, and some outcomes were not reported. There was no justification for any missing outcomes or clarification on methods.

Limitations of the evidence base include relatively outdated studies, low quantity and quality of studies, and small sample sizes in the identified studies. The uncertainty in the evidence and the identified studies means that the conclusions from these studies should be interpreted with caution.

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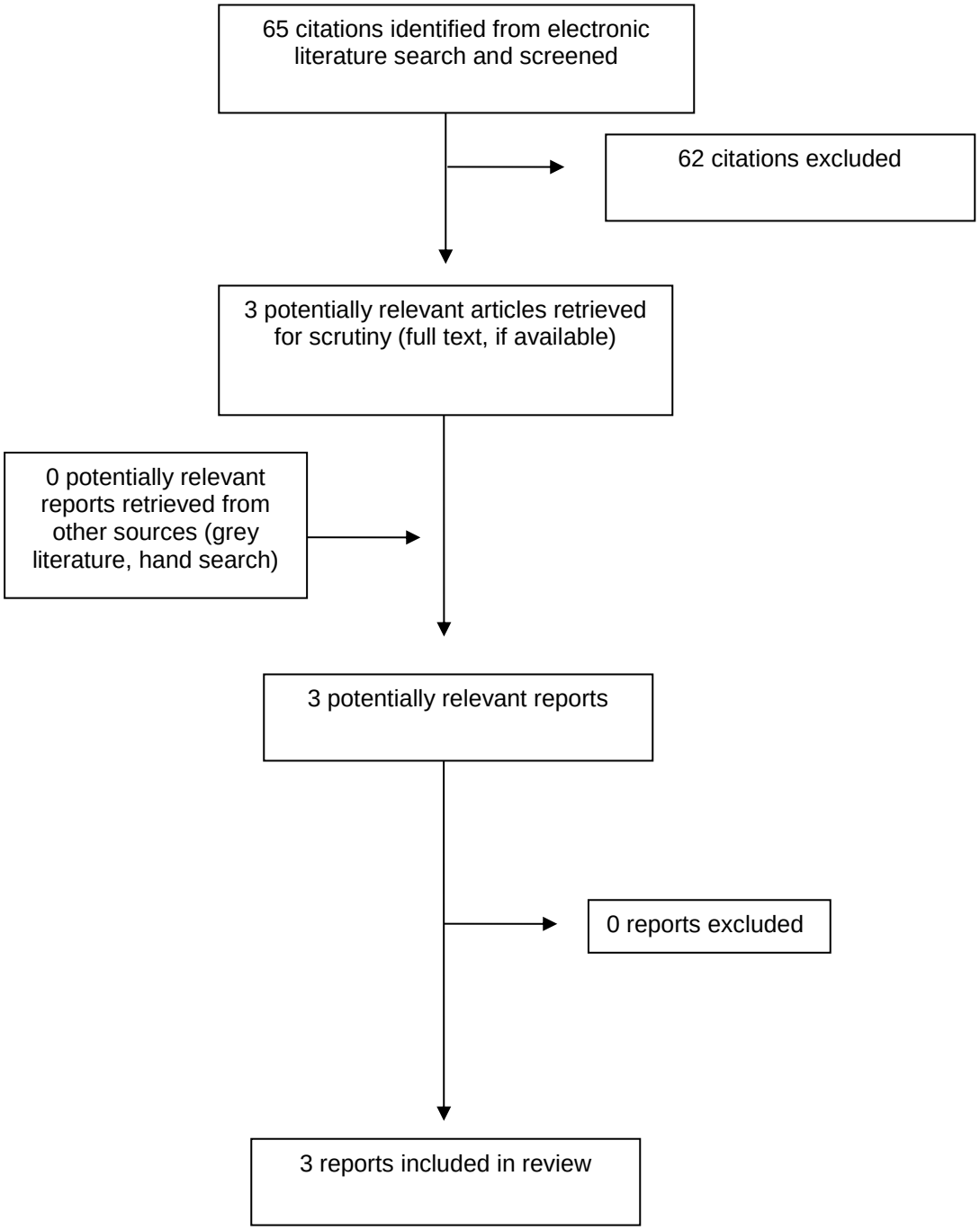
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Forbat et al[2] **Australia** **Internship program of the Australian Catholic University**	English studies only Eligible study designs NR *Databases:* CENTRAL, Medline, EMBASE, Web of Science, CINAHL *Number of primary studies:* N = 14 studies Hospices: n = 8 Long stay unit: n = 6 *Relevant to this report:* n = 2	Adults (>18) with advanced illness who received SC hydration of fluids, including patients in residential facilities or "aged care facilities" (i.e., long term care) who are receiving generalist palliative care	*Intervention:* HDC *Comparator:* IV fluids	*Outcomes:* NR For HDC, identified studies included complications of treatment *Length of Follow-up:* NR
Duems-Noriega and Ariño-Blasco 2015[1] **Spain** Funding NR	"Original articles", reviews, letters to the editor, or communications, no limit on publication year or language *Databases:* CINAHL, EMBASE, PubMed and Cochrane library *Number of primary studies:* N = 178 *Relevant to this report:* n = 3	Eligible population not specified, but likely any patient requiring SC administration of drugs or fluid	*Intervention:* HDC with fluids or; SC administration of drugs (ketorolac, morphine, ceftriaxone, analgesics, opioids, antibiotics) *Comparator:* NR, assumed all comparators	*Outcomes:* NR for methods For HDC of fluid, identified studies included outcomes such as urea levels, creatinine levels, serum sodium levels, discomfort, feasibility, osmolarity, function *Length of Follow-up:* NR

CENTRAL = Cochrane Central Register of Controlled Trials; CINAHL = Cumulative Index to Nursing and Allied Health Literature; EMBASE = Excerpta Medica database; HDC = hypodermoclysis; IV = intravenous; NR = not reported; SC = subcutaneous; SD = standard deviation.

Table 3: Characteristics of Included Primary Clinical Studies

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Esmeray et al 2018[8] **Turkey** Funding NR	RCT with a crossover design Randomization done by a "a randomized drawing method" Three intervention infusions and three control infusions were done on the same patient, with randomization performed to determine the order in which the infusion was done (i.e., control first, then intervention, or intervention first, then control)	Geriatric patients (> 65 years) in private long-stay care unit with a daily fluid intake of less than 1000mL, mild to moderate dehydration, no difficulty in swallowing but insufficient fluid intake, requiring parenteral nutrition, symptoms of dehydration. Excluded patients with infection, skin issues, acute dehydration, edema, and individual receiving IV medication or total parenteral nutrition *Age, mean (SD)* 81.97 (8.81) *Sex* 90% female 66.7% dependent on nutritional support 60% dependent on fluid intake support 56.7% fed orally 66.7% bed-bound	*Intervention:* Three consecutive HDC infusions, 125 mL/hour, 1000mL of 0.9% saline solution with 21- to 23-gauge SC infusion butterfly needles in abdomen *Comparator* Three consecutive IV infusions	• Complications (i.e., edema, redness, bleeding, and agitation) • Use of consumables • Urine density • pH values of urine • Vital signs

HDC = hypodermoclysis; IV = intravenous; NR = not reported; SC = subcutaneous; SD = standard deviation.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Systematic Reviews Using AMSTAR 2[5]

Strengths	Limitations
Forbat 2016[2]	
• Aim of the review clearly stated • Review registered in PROSPERO prior to conducting search • Preliminary searches done to determine appropriate inclusion and exclusion criteria • Multiple databases used (CENTRAL, Medline, EMBASE, Web of Science, CINAHL), and an example search provided • Clear inclusion and exclusion criteria • Standardized form used to extract data • Two review authors extracted data for review • Both abstracts and full text screened by two review authors	• Some results missing from tables, e.g., clinical outcomes for HDC • No excluded studies list • No sources of funding reported for the primary studies • Only searched for English language papers • Eligible study designs were unclear
Duems-Noriega and Ariño-Blasco[1]	
• Used MeSH headings for the search • Searched through a variety of databases (CINAHL, EMBASE, PubMed and Cochrane library) • Conflicts of interest statement provided	• Inclusion criteria is unclear and research questions not specified. There is no clear population group, intervention, comparison, or outcomes that were eligible for inclusion. • The report mentions methodological shortcomings but does not specify if any tool or method was used to assess the studies • Results from studies not complete – there are no ages, sexes, specific settings, rate of infusion, or type of infusion noted • There is no protocol or indication of SR registration • There is no information on study selection (full text or abstract) or data extraction • The authors do not state how many papers were identified in the search therefore it is unclear if the search parameters yielded an expected number of studies • Unclear what the search dates for the review are (i.e., no limits on date, but unclear what date the search was performed) • No sources of funding reported for the primary studies or SR • No excluded studies list

CENTRAL = Cochrane Central Register of Controlled Trials; CINAHL = Cumulative Index to Nursing and Allied Health Literature; EMBASE = Excerpta Medica database; HDC = hypodermoclysis; PROSPERO = prospective register of systematic reviews; SR = systematic review.

Table 5: Strengths and Limitations of the Included Clinical Study Using the Downs and Black checklist[6]

Strengths	Limitations
Esmeray 2018[8]	
• Objective of study clear • Appropriate paired statistical tests were used as the individuals acted as their own controls (McNemar's, Wilcoxon signed rank) • Actual probability values are stated • Characteristics of patients described • Care likely representative of care received for majority of patients, and patient likely representative of older patients in care homes in Turkey	• Interventions are not fully detailed – e.g., the IV administration is not explained fully, and there is no detail on how far apart the "consecutive" administrations of hydration were. There is no detail on how long there was between administration of HDC and IV fluids, or vice versa • The randomization technique is not discussed in detail. It is unclear what was used to determine the order of administration for the patients • The outcomes to be measured are provided, but how these were measured is unclear – e.g., what scales were used, or what threshold was used to determine whether an effect was considered an adverse event and noted • Unclear why bleeding, edema, redness, and agitation were the only AEs studied • Unclear why some reported outcomes in the methodology are not reported in the results • Unclear whether anyone (patients or assessors of outcomes) were blinded to treatment. It is unlikely to have been possible to blind the individual providing the treatment as the administration technique differs significantly • Unclear if allocation was concealed • No power calculation

AE = adverse events; HDC = hypodermoclysis; IV = intravenous.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 6: Summary of Findings for Included Systematic Reviews

Main study findings	Authors' conclusion
Forbat 2016[2]	
N = 2 **"Evidence for administering HDC"** *1 SR (Frisoli et al 2000, low quality)[a:]* Most studies used drip rate of 15 to 75 mL/h or gravity-based drip rate Frequency and duration NR • Concludes that HDC is safe and effective for older people with mild to moderate dehydration, but does not provide any statistical tests or numbers **IV Hydration vs. HDC** ***Frail elderly:*** *1 prospective observation study (Dasgupta et al 2000, high quality)[a:]* n = 55 Infusion rate 20 to 75 mL/h, daily or "as required" for 21 days Mean age (SD): 83.5 (10.5) Sex: 40% female, 60% male • Fluid related complications lower in HDC group compared with IV, P = 0.04	*The need to determine best practice in all forms of care for people with advanced life-limiting illness is increasingly pressing, in the context of the demographic profile of ageing populations. Hydration necessarily will be part of this, including determining best modes of delivery of HDC." p. 1213* *"Further, there is currently limited evidence (and none available from the papers in this review) regarding site use duration, the need for site rotation, choice of administration method and its relationship with adverse reactions (e.g. by pump in the anterior abdominal wall). Further, there was no available evidence on appropriate methods of HDC in populations whose symptoms contribute to complexities in administration (such as people with behavioural and social symptoms of dementia, or delirium). Further research into the appropriate methods of HDC is additionally required to progress understanding of the efficacy and suitability of this practice. The absence of an accepted approach to HDC contributes to the difficulties in constructing an evidence base for efficient practice within populations with advanced illness." p. 1213*
Duems-Noriega and Ariño-Blasco[1]	
N = 3 **One study overlapped with Forbat 2016[2]** This study was Dasgupta et al,[9] examining frail patients receiving HDC or IV fluid. Some details are above. Forbat et al[2] did not include some information regarding this study that this SR did include, i.e.: • General/clinical improvement was not different between groups (P = 0.19) • Local reactions were lower in HDC (P = 0.02) **No comparator (before and after)** *1 uncontrolled study, care home residents (Hussain and Warshaw 1996)* n = 36, age NR • No improvement in serum sodium or urea/creatinine levels (P = NR) • 71% returned to a functional or clinical baseline (P = NR) *1 uncontrolled prospective study, frail elderly patients (Arinzon et al 2004)* n = 57 • 77% had clinical improvement (P = NR) • Urea levels improved (P = 0.001) • Creatinine levels improved (P < 0.001)	*"Despite many prejudices and initially discouraging results mostly related to poor technique, SC rehydratrion [sic] (or hypodermoclysis) is now accepted as an effective fluid replacement method in mild to moderate dehydration, with bioequivalence to IV infusion and restoration of biochemical parameters, excellent tolerance, easy placement and minimal risk in situations where other routes have been shown to be ineffective." p. 120 - 121*

Main study findings	Authors' conclusion
• Sodium levels improved (P < 0.05)	

h = hour; HDC = hypodermoclysis; IV = intravenous; mL = millilitres; NR = not reported; SC = subcutaneous; SD = standard deviation; SR = systematic review.

[a] According to authors of the SR (Forbat 2016[2]).

Table 7: Summary of Findings of the Included Clinical Study

Main study findings	Authors' conclusion
Esmeray 2018[8]	
Demographics: **N = 30** *Age, mean (SD)* 81.97 (8.81) *Sex* 90% female 66.7% dependent on nutritional support 60% dependent on fluid intake support 56.7% fed orally 66.7% bed-bound **Complications** *All complications, all administration times* HDC vs. IV, n (%) 10 (11.1) vs. 68 (75.6) **P = 0.001** *Redness* HDC vs. IV, n (%), 1st administration 7 (23.3) vs. 27 (90.0) **P = 0.001** HDC vs. IV, n (%), 2nd administration 15 (50.0) vs. 19 (63.3) P = 0.481 HDC vs. IV, n (%), 3rd administration 14 (46.7) vs. 21 (70.0) P = 0.143 HDC vs. IV, n (%), Total 36 (40.0) vs. 67 (74.4) **P = 0.001** *Agitation* HDC vs. IV, n (%), 1st administration 2 (6.7) vs. 24 (80.0) **P = 0.001** HDC vs. IV, n (%), 2nd administration 5 (16.7) vs. 22 (73.3) **P = 0.001** HDC vs. IV, n (%), 3rd administration 3 (10.0) vs. 22 (73.3) **P = 0.001**	*"In the current study that investigated the efficacy of HDC for hydration treatment of geriatric patients, IV and SC infusion approaches, which revealed that side effects were significantly fewer with HDC (Table 2)." p. 443* *Catheters were inserted via the SC route in less than half the time it took for IV insertion, which can enhance the comfort of the patient compared with the IV infusion and positively affect the nursing labour force. With SC infusion, catheter duration time is approximately 2–2.5 times the time with IV infusion, which is suitable for providing a longer duration of hydration." p. 444* *"In the current study, the number of catheters used in IV infusion was significantly higher than that used in the SC infusion (Table 3, p<0.001). Catheter cost was also lower with HDC than IV infusion. These findings are also important for healthcare policies in the search for effective, safe and affordable approaches. Similar results demonstrating that HDC might be more affordable were also reported by numerous studies" p. 444*

Main study findings	Authors' conclusion
HDC vs. IV, n (%), Total 10 (11.1) vs. 68 (75.6) **P = 0.001** *Edema* HDC vs. IV, n (%), 1st administration 4 (13.3) vs. 6 (20.0) P = 0.754 HDC vs. IV, n (%), 2nd administration 0 vs. 8 (26.7) P = NA HDC vs. IV, n (%), 3rd administration 0 vs. 6 (20.0) P = NA HDC vs. IV, n (%), Total 4 (4.4) vs. 20 (22.2) **P = 0.002** *Bleeding* HDC vs. IV, n (%), 1st administration 6 (20.0) vs. 26 (86.7) **P = 0.001** HDC vs. IV, n (%), 2nd administration 2 (6.7) vs. 19 (63.3) **P = 0.001** HDC vs. IV, n (%), 3rd administration 3 (10.0) vs. 21 (70.0) **P = 0.001** HDC vs. IV, n (%), Total 11 (12.2) vs. 66 (73.3) **P = 0.001** **Number of catheters used** HDC vs. IV, mean (SD), 1st administration 1.20 (0.41) vs. 2.033 (0.96) **P = 0.001** HDC vs. IV, mean (SD), 2nd administration 1.07 (0.25) vs. 2.033 (1.00) **P = 0.001** HDC vs. IV, mean (SD), 3rd administration 1.10 (0.31) vs. 2.67 (3.42) **P = 0.001** HDC vs. IV, mean (SD), Total 1.12 (0.33) vs. 2.04 (0.97) **P = 0.001** **Catheter duration (hour)** HDC vs. IV, mean (SD), 1st administration 39.20 (12.97) 18.27 (15.85) **P = 0.001** HDC vs. IV, mean (SD), 2nd administration 24.87 (11.69) 12.83 (11.52) **P = 0.001** HDC vs. IV, mean (SD), 3rd administration	

Main study findings	Authors' conclusion
33.07 (12.60) 14.03 (10.70) **P = 0.001** HDC vs. IV, mean (SD), Total 32.38 (13.63) 15.04 (12.96) **P = 0.001** **Catheter insertion time (minute)** HDC vs. IV, mean (SD), 1st administration 1.90 (0.31) 5.83 (2.61) **P = 0.001** HDC vs. IV, mean (SD), 2nd administration 1.47 (0.51) 4.77 (3.39) **P = 0.001** HDC vs. IV, mean (SD), 3rd administration 1.60 (0.50) 5.82 (4.50) **P = 0.001** HDC vs. IV, mean (SD), Total 1.66 (0.48) 5.47 (3.58) **P = 0.001**	

h = hour; HDC = hypodermoclysis; IV = intravenous; mL = milliliters; n = number; SC = subcutaneous; SD = standard deviation.

Appendix 5: Overlap between Included Systematic Reviews

Table 8: Overlap in Relevant Primary Studies between Included Systematic Reviews

Primary study citation	Systematic review citation	
	Forbat et al[2]	Duems-Noriega and Ariño-Blasco 2015[1]
Arinzon et al 2004[10]		x
Dasgupta et al 2000[9]	x	x
Frisoli et al 2000[11]	x	
Hussain and Warshaw 1996[12]		x

Appendix 6: Further Information

Previous CADTH Reports

1. Prevention of dehydration in geriatrics in long-term care: guidelines. *(CADTH rapid response report: summary of abstracts).* Ottawa (ON): CADTH; 2017 Jun. https://cadth.ca/prevention-dehydration-geriatric-patients-long-term-care-guidelines-0. Accessed 2020 Aug 28.

2. Prevention of Dehydration in Geriatric Patients in Long-Term Care: Guidelines. *(CADTH rapid response report: summary of abstracts).* Ottawa (ON): CADTH; 2014. https://cadth.ca/prevention-dehydration-geriatric-patients-long-term-care-guidelines. Accessed 2020 Aug 28.

3. Volume and Site Preferences for Hypodermoclysis: A Review of Clinical Practice Guidelines. *(CADTH Rapid response report: Health Technology Inquiry Service).* Ottawa (ON): CADTH; 2010. https://cadth.ca/volume-and-site-preferences-hypodermoclysis-review-clinical-practice-guidelines-0. Accessed 2020 Aug 28.

Systematic Review Articles – Out of Date Range

4. Rochon PA, Gill SS, Litner J, Fischbach M, Goodison AJ, Gordon M. A systematic review of the evidence for hypodermoclysis to treat dehydration in older people. J Gerontol A Biol Sci Med Sci. 1997;52(3):M169-176. PubMed: PM 9158559

Additional References

5. Food Fluid & Nutritional Care (FFNC) Policy Review Group. Food, Fluid and Nutritional Care Policy. *(Clinical Policy)*. Dundee (UK): NHS Tayside. 2018. https://www.nhstaysidecdn.scot.nhs.uk/NHSTaysideWeb/idcplg?IdcService=GET_SECURE_FILE&Rendition=web&RevisionSelectionMethod=LatestReleased&noSaveAs=1&dDocName=prod_224033. Accessed 2020 Aug 28.

6. Hypodermoclysis (HDC) Administration. *(Corporate Policy & Procedures Manual)*. Edmonton (AB): Covenant Health. 2017. http://extcontent.covenanthealth.ca/Policy/VII-B-315.pdf. Accessed 2020 Aug 28.

7. Best Practices for Nutrition, Food Service and Dining in Long Term Care Home: A Working Paper of the Ontario LTC Action Group. Toronto (ON): Dietitians of Canada. 2019. https://www.dietitians.ca/DietitiansOfCanada/media/Documents/Resources/2019-BestPractices-for-Nutrition,-Food-Service-and-Dining-in-Long-Term-Care-LTC-Homes.pdf. Accessed 2020 Aug 28.