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# Lower costs for collagenase injections than fasciectomy in the treatment of Dupuytren's contracture: A single-centre controlled cohort study

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## Abstract

**Objectives**: The aim of this controlled cohort study of Dupuytren's contracture (DC) was to compare collagenase injections with surgery (fasciectomy) with regard to the actual total direct treatment costs and short-term outcomes.

**Setting**: Orthopaedic department of a regional hospital in Sweden.

**Participants**: Patients aged 65 years or older with previously untreated DC of 30 degrees or greater in the metacarpophalangeal (MCP) or proximal interphalangeal (PIP) joints of the small, ring or middle finger. The collagenase group comprised 16 consecutive patients treated during the first 6 months following the introduction of collagenase as treatment for DC at the study centre. The controls were 16 patients randomly selected among those operated on with fasciectomy at the same centre during the preceding 3 years.

**Interventions**: Treatment with collagenase was given during two standard outpatient clinic visits (injection and next-day finger extension under local anaesthesia) followed by night-time splinting. Fasciectomy was done in the operating room (day surgery) under general or regional anaesthesia using standard technique, followed by therapy and splinting.

**Primary and secondary outcome measures**: Actual total direct costs (salaries of all medical personnel involved in care, medications, materials and other relevant costs), and total MCP and PIP extension deficit (degrees) measured by hand therapists at 6-12 weeks after treatment.

**Results**: Collagenase injection required fewer hospital outpatient visits to a therapist and nurse than fasciectomy. Total treatment cost for collagenase injection was 1418.04 USD and for fasciectomy 2102.56 USD. The post-treatment median (interquartile range) total extension deficit was 10 (0-30) for the collagenase group and 10 (0-34) for the fasciectomy group.

**Conclusions**: Treatment of Dupuytren's contracture with collagenase injection costs 33% less than fasciectomy with equivalent short-term efficacy regarding reduction in contracture.

**Strengths and limitations of this study**

- This study presents previously unknown estimates of the actual costs of treating Dupuytren's contracture with Collagenase injections or fasciectomy
- Comparison of the actual costs of the two treatments are based on detailed definition and measurement of all relevant costs
- Outcomes of injections were prospectively measured but outcomes of surgery were based on medical records
- Costs may vary across countries
- Only short-term outcomes were compared

## INTRODUCTION

Dupuytren's contracture (DC) is a common hand disorder causing finger contractures that may compromise hand function. Surgery in the form of limited fasciectomy has been the main treatment option for reducing the contracture.[1] In Sweden (population 9.5 millions), more than 3000 fasciectomy procedures are performed annually;[2] the actual number is probably higher because procedures performed by surgeons in private practice, although constituting a small proportion,[3] may not always be reported to the national database. Surgery is usually done in the main operating room under general or regional anaesthesia and the operating time is on average about 1 hour,[4] but can be substantially longer when severe contractures are present in multiple fingers. After surgery many patients require therapy and splints. Although surgery is often effective in reducing the contracture, postoperative complications such as nerve injury and wound healing problems are common and patients may develop contracture recurrence.[5,6]

Recently, injection with collagenase clostridium histolyticum (CCH) has been introduced as the first pharmacological treatment for DC after it was shown in a randomized controlled trial to be more effective than placebo injections in reducing contractures.[7] The treatment is a relatively simple procedure given in the outpatient clinic and rarely requires prolonged therapy. The current price of a CCH injection (in Sweden) is almost one thousand US dollars (USD) and one injection is used for each finger involved (unless contractures in 2 fingers are caused by a common cord). Because of economic pressure to control health care expenditures, the cost-effectiveness of surgical procedures has gained increased significance in hospital decision making. The cost analysis of different treatment procedures such as fasciectomy and

injection is therefore essential and the differences in short-term costs associated with these two techniques are important to consider.

To our knowledge no previous study has compared the actual costs of CCH injections with those of fasciectomy. One study based on a cost-utility analysis model concluded that open partial fasciectomy did not meet the cost-effectiveness threshold and that CCH injections would be cost-effective when priced below 945 USD.[8] Studies concerning costs of surgery have usually used reimbursement as a measure of costs,[9] but reimbursement does not necessarily reflect the actual cost of a procedure. Reimbursement levels for a certain procedure may vary substantially across and even within countries. For cost comparison of CCH injections and fasciectomy in DC the actual cost of each procedure is therefore a more relevant measure. When comparing the costs of two treatment methods, the outcome of the treatments must also be taken into consideration. However, we could not find studies that have compared the outcomes of CCH and fasciectomy.

The main aim of this controlled cohort study was to compare CCH injections with fasciectomy regarding the actual total direct treatment costs. The secondary aim was to compare the short-term outcomes of these two treatment methods.

## PATIENTS AND METHODS

### Study participants

We conducted a controlled cohort study at one orthopaedic department (Hässleholm, Kristianstad and Ystad Hospitals) in southern Sweden. The department is the only centre that treats patients with DC in a region with approximately 300,000 inhabitants.

Data on CCH injections were collected prospectively within a clinical study that started September 2011 when CCH was introduced as the main treatment option for DC at the department. The indication for treatment with CCH injections was identical to that previously used for surgery at the study centre, namely a palpable cord and contracture of 30 degrees or greater in the metacarpophalangeal (MCP) or proximal interphalangeal (PIP) joints. For this study we included the first 16 consecutive patients, aged 65 years or older, treated with CCH injections during the first 6 months (September 2011 through February 2012). We restricted the study to patients of non-working age because we aimed to compare only direct costs.

Data on fasciectomy were extracted from the medical records of patients treated at the department before the introduction of CCH injections. The patients were chosen among those aged 65 years or older, operated on with fasciectomy January 2009 through June 2011. Patients with surgery on more than 2 fingers, previous surgery for DC in the same hand, and additional procedures performed (e.g. skin graft or amputation) were excluded. A total of 113 patients were potentially eligible. Of these, a random sample of 15% was chosen by computer (statistical software), yielding 18 patients; 2 were excluded (1 had surgery for DC in the thumb and 1 chose to have postoperative therapy at another location). Thus, the fasciectomy group included 16 patients.

**Treatment and follow-up procedures**

Both treatments required an initial standard outpatient consultation visit to a hand surgeon or an orthopaedic surgeon, usually as a referral from the patient's general practitioner. Each surgeon was assisted by a nurse at the outpatient clinic. During the visit the treatment decision was made and the patient was scheduled for treatment (Fig 1).

***Collagenase injection***: Treatment with CCH required two standard outpatient visits to a hand surgeon: injection and next-day finger extension under local anesthesia.[7] During these visits the surgeon was assisted by a nurse (all treatments were given by the same hand surgeon). Immediately after finger extension the patient went to the therapist and received a splint for use at night for 8 weeks. A second visit to the therapist was done 1 week post-injection for splint adjustment and therapy instructions. Patients who during finger extension developed a skin tear that was judged to require dressing change were asked to visit a nurse within 2 to 3 days. Further visits to the nurse were done when necessary, depending on wound status. No routine post-treatment visits were scheduled to the treating surgeon and the final follow-up (usually at 5-6 weeks) was done by the therapist who arranged a consultation to the treating surgeon if necessary (consideration for further treatment).

***Fasciectomy***: Fasciectomy was done as a day-surgery procedure in the main operating room (OR). The surgery was done by one of six different surgeons (three experienced hand surgeons and three orthopaedic surgeons with experience in hand surgery) using standard technique for limited open fasciectomy.[10] General anaesthesia or axillary block was used. According to routine procedures at the hospital general anaesthesia was administered by a nurse anaesthetist and axillary block was administered by an anaesthesiologist, after which the nurse anaesthetist was in charge of the patient's care with anaesthesiologist help obtained

when needed. The surgery was done by a surgeon (no assistant) with a team consisting of an OR nurse, a nurse anaesthetist and 2 nurse assistants (1 participated only in the initial preparations). The electronic records for each surgical procedure include the exact start and finish times for the preparations before surgery, anaesthesia, the actual surgery (i.e. operating time from incision to dressing), and the work done after the surgeon has completed the operation and until the patient is taken back to the recovery room. After returning from the OR the patient stayed in the recovery room until discharge from the day-surgery unit. The time of discharge is documented in the electronic records. Thus, for each patient 3 times were recorded; the operating time, the total OR time (from start of preparations until room ready for next procedure), and the time at the recovery room until discharge.

After fasciectomy all patients visited a nurse for dressing change after 5 to 7 days, followed immediately by a visit to a therapist for a splint and therapy instructions. A second visit to the nurse for wound inspection and suture removal was done at approximately 2 weeks. Further visits to the nurse were done when necessary, depending on wound status. Patients also had further visits to the therapist for scar management, splint adjustments and therapy instructions as required. The treating therapist decided on the frequency and duration of therapy. Patients had 1 postoperative follow-up visit to the surgeon timed according to surgeon preference.

**Cost measurement**

A detailed analysis of the salaries of physicians and non-physician medical personnel involved in the treatment of patients with DC was performed for CCH injection and fasciectomy. We identified the average salaries of individuals and used the average time units to calculate the cost of manpower. The costs of all materials, premises and other costs were calculated. We included fixed assets such as the costs of the premises and its expenses and the

costs of surgical equipment. All costs were measured based on 2011 salaries/prices. These costs include; salaries of all medical personnel involved in the direct care of the patients including social security contributions, vacation pay and sick pay (averaged for each category: specialist orthopaedic surgeon, anaesthesiologist, nurse, nurse assistant and therapist), hospital overhead costs, the degree of capacity utilization, medications, surgical and other material, premises and other costs. The average salaries were based on all respective medical personnel group in the public health care sector in the region. We did not include costs of non-medical personnel involved in the care (such as receptionists, secretaries, cleaners, etc).

A standard outpatient visit to a doctor was 20 minutes. For the 2 CCH visits (injection and finger extension) we used the standard time for the surgeon and 25 minutes for the assisting nurse (to account for the time needed for preparations and work after the session had ended). For fasciectomy we used the mean operating time, total OR time and recovery time, according to the personnel involved and adjusted as required. For the operating surgeon we used the mean operating time plus 25 minutes needed for additional work (assessing the patient and marking the surgical site before surgery, scrubbing, writing the surgical notes and discharging the patient after surgery). For the non-physician personnel we used the mean total operating room time and for the anaesthesiologist we used half that time (one anaesthesiologist is usually assigned to 2 operating rooms simultaneously and the care of these patients after surgery). For recovery room personnel (a nurse and a nurse assistant are in charge of up to 5 patients simultaneously), we used a fifth of the recovery time plus 5 minutes (preoperative preparations). A standard outpatient visit to a nurse (for wound care after CCH injection or fasciectomy) was 45 minutes. A standard visit to therapist after CCH injection was 30 minutes and after fasciectomy 45 minutes. For each patient the exact number of hospital

outpatient visits to a doctor, nurse or therapist, related to the treatments, was retrieved from the Patient Administrative System.

**Outcome measurement**

At baseline and at all follow-up visits range of motion including extension and flexion of the MCP and PIP joints of the fingers was measured with a goniometer. In the fasciectomy group the baseline measurements were done by the surgeons during the visit that resulted in the patient being scheduled for fasciectomy and the post-treatment measurements were done by six different therapists; these measurements were recorded in the patient's electronic medical records. In the CCH group all measurements (immediately before injection and at follow-up) were done by the same therapist, as part of a research project. The measurements recorded at baseline and at the final visit were used in the analysis.

**Analysis**

In 2 previous randomized trials the proportion of MCP joints that were reduced to 0 to 5 degrees of extension deficit was 45% at 30 days after first CCH injection[7] and 94% at 6 weeks after fasciectomy.[11] To detect a difference of this magnitude between the 2 groups (80% power and 0.05 significance level) would require a sample of 13 patients in each group. The cost estimation of CCH was based on standard procedures independent of sample size. For the cost of fasciectomy, a random sample of 15% from 113 fasciectomy-treated patients was judged adequate to provide representative average procedure time estimates and number of visits to medical personnel, on which the total cost was based. Data are shown as mean and SD and/or median and interquartile range (IQR). We calculated the average total cost of treatment per patient when only 1 CCH injection is required. We also calculated the cost if 20% of the patients would require 2 CCH injections given on separate sessions to obtain

contracture reduction. Because some patients who developed skin tears during finger extension chose to have dressing change, when necessary, at home or at primary care, only 1 nurse visit was recorded in the Patient Administrative System. We therefore made the calculations assuming 1 of 3 patients in the CCH group would require 1 nurse visit. We also conducted a sensitivity analysis with the conservative assumption of 1 nurse visit per patient. All costs were calculated in Swedish Kronor (SEK) and converted to USD using the rate of 1 USD = 6.676 SEK (Sweden's Central Bank average for 2011). The within-group change in extension deficit was analyzed with the Wilcoxon test. We also compared the 2 groups with regard to improvement in total extension deficit using the Mann-Whitney test. A p value below 0.05 was used to indicate statistical significance.

## RESULTS

The 16 patients in the CCH group and the 16 patients in the fasciectomy group had similar characteristics (Table 1). In the fasciectomy group half of the patients received general anaesthesia and the other half axillary block. The mean operating time was 62 (SD 27) minutes, mean total OR time 138 (SD 43) minutes, and mean postoperative time spent at the day-surgery recovery room until discharge 215 (SD 41) minutes. The median time from surgery to end of therapy was 6.3 weeks (IQR 4.0-11.5) and to the postoperative follow-up by the surgeon 7.5 weeks (IQR 6.0-12.0). None of the patients in the CCH group required further therapy than the standard visits. Of the 16 patients, 9 developed skin tears ranging from minor superficial skin breakage that did not require further wound care to deeper wound that required 1 or more dressing changes. All wounds had healed within 2 weeks after injection.

### Costs

The cost specifications for the two treatments are shown in Table 2. The largest treatment cost for CCH injections was the cost of the injection itself (970.19 USD) and for fasciectomy the cost of personnel (783.97 USD) and other costs (380.81 USD) associated with the surgery in the operating room. Compared to fasciectomy, treatment with CCH injections required fewer outpatient hospital visits to a nurse and a therapist (Table 3).

The total treatment cost with 1 CCH injection was 33% lower than that for fasciectomy (1418.04 versus 2102.56 USD). The cost was still lower (1675.24 USD) if 20% of patients treated with CCH would require 2 injections in the same hand, given in separate sessions. In the sensitivity analysis the cost of CCH injections assuming an average of 1 nurse visit per

patient was 1472.51 USD when 1 injection is given and 1696.79 USD when 20% would require 2 injections.

**Outcomes**

Of the 16 patients in the CCH and fasciectomy groups, 7 and 9 patients respectively achieved an extension deficit of 0 to 5 degrees in the joint with the largest extension deficit. In both groups the improvement in total extension deficit was statistically significant ($p < 0.001$) and the extension deficits after CCH and fasciectomy were similar (median 10 degrees) (Table 3). The median improvement in total extension deficit in the CCH group was 70 (IQR 55-85) degrees and in the fasciectomy group 50 (IQR 41-60) degrees ($p=0.006$).

No complications were observed in any of the groups at the final follow-up.

## DISCUSSION

Our study shows that treatment of DC with collagenase injections is associated with lower costs than surgery (fasciectomy) and results in similar short-term outcomes regarding reduction in finger joint contractures. The costs are still lower when assuming that 20% of the patients would require 2 injections in the same hand, but if more than 5 of 10 patients need 2 or more injections the costs would exceed those of fasciectomy. Our estimates of the costs assuming 20% would require 2 injections were based on separate treatment sessions; the costs would be even lower if the 2 injections are given in the same session, which would probably become the usual practice.[12] Further, our results should be considered conservative since we have not considered complications (such as wound infection and chronic regional pain syndrome) that are probably more frequent after surgery than after CCH injections and would therefore add to the total costs.

For fasciectomy, the largest cost was represented by the various costs associated with a day-surgery procedure of approximately 1 hour duration in the operating room. The cost would be lower if the average operating time were shorter than our estimate of 62 minutes. In a recent study of DC in 12 European countries (based on a surgeon survey and patient chart review), the mean operating time for fasciectomy across all countries was 67 minutes (Nordic 63, Eastern 69, Western 66, and Mediterranean 68 minutes).[4] A potential advantage with CCH injections is the possibility to treat patients with bilateral disease in 1 stage, which is uncommon with surgery considering the nature of the procedure. In contrast, patients with contractures involving 3 or more fingers can be treated with surgery in one session, but would need at least 2 CCH injections and, in more severe cases, 2 or more treatment sessions.

Skin tears ranging from minor superficial skin breakage to deeper wounds occurred in more than half the patients after CCH injections in our study. Skin tears following CCH injections were reported in 11% in the multicenter randomized trial,[7] and in up to 19% in other studies.[13,14] Skin tears are more likely to occur in severe contractures especially of the small finger.[9] Because the incidence and severity of skin tears (ie, need for wound care) may vary we calculated the costs assuming that, on average, one third of the patients would require 1 nurse visit and also did a sensitivity analysis assuming an average of 1 nurse visit. We believe these estimates cover the costs of wound care even if the true incidence of skin tears is higher than previously reported.

We only compared direct costs, and therefore did not include costs of lost productivity or sick leave. Among employed patients, sick leave is more likely to be necessary and longer after fasciectomy than after CCH injections. According to the Swedish Social Insurance Agency the total cost of a 1-week sick leave based on the average salary in Sweden 2011 (including sick-pay, general payroll tax, vacation-pay and overhead costs) exceeds 1300 USD (www.scb.se). In addition, the direct costs of CCH injections and fasciectomy may differ across countries and settings. In a Canadian study that estimated the cost (during 2005) of open carpal tunnel release, a 10-minute procedure done under local anaesthesia, the total cost (excluding surgeon's fee) was 137 CAD when done in the main operating room and 53 CAD dollars when done in the office.[15]

A limitation of our study is that only short-term outcomes were measured. The improvement was high and the minor residual contracture was similar for CCH and fasciectomy. Differences in long-term outcomes may change the cost-effectiveness of these treatments

because if they differ substantially in the recurrence rate and the need for further treatments the cost of subsequent treatments should also be considered. According to the most recent estimate of recurrence following CCH injections, the rate at 5 years was 35% but in only 7% the recurrence required treatment.[16] Another limitation is that in the fasciectomy group the baseline range-of-motion measurements were done by different surgeons and the follow-up measurements by different therapists. The inter-observer reliability of these measurements is unknown and there might be a risk that the surgeon overestimated the preoperative contracture and the treating therapist underestimated residual contracture. However, we do not believe this issue has a substantial influence because fasciectomy was the only treatment option and the results of the post-treatment measurements, done by therapists, were similar in both groups.

In conclusion, treatment of DC with CCH injections costs 33% less, in direct costs, than fasciectomy with equivalent short-term efficacy regarding reduction in contracture.

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**Contributorship Statement**

ES, AL, IA: Study conception and design, acquisition of data, analysis and interpretation of data, and drafting of the article.

EA: Acquisition of data, and critical revision of the article for important intellectual content.

MW: Analysis and interpretation of data and critical revision of the article for important intellectual content.

All authors approved the final submitted version.

**Competing Interests**

Dr. Atroshi was a member of an Expert Group on Dupuytren's disease for Pfizer 2012. The other authors have no competing interests.

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**Table 1.** Characteristics of the two samples of patients with Dupuytren's contracture treated with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | CCH injection | Fasciectomy |
|---|---|---|
| Number of patients (men) | 16 (11) | 16 (13) |
| Age (yrs), mean (SD) | 69 (4) | 71 (5) |
| Number of fingers treated* | | |
| Small | 11 | 9 |
| Ring | 7 | 8 |
| Middle | 0 | 1 |
| Total extension deficit (degrees)† | | |
| mean (SD) | 90 (39) | 71 (28) |
| median (IQR) | 70 (60-115) | 75 (45-89) |

CCH, collagenase clostridium histolyticum; IQR, interquartile range

*2 patients in each group had 2 fingers treated.

† Metacarpophalangeal (MCP) plus proximal interphalangeal (PIP) joints (no MCP contracture in 1 patient in the CCH group and 2 patients in the fasciectomy group and no PIP contracture in 7 patients and 4 patients, respectively). In patients with 2 fingers treated the largest extension deficit was used.

**Table 2.** Cost specification for the various stages of treating Dupuytren's contracture with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | **Personnel costs** * (USD) | **Other costs** † (USD) |
|---|---|---|
| Doctor visit, CCH or fasciectomy (doctor and nurse) | 65.80 | 16.78 |
| Injection, CCH (doctor and nurse) | 70.63 | 991.16 |
| Finger extension, CCH (doctor and nurse) | 70.63 | 20.97 |
| Therapist visit, CCH | 26.58 | 25.16 |
| Surgery, fasciectomy (doctors and others) | 783.97 | 380.81 |
| Day surgery care, fasciectomy | 88.10 | 52.41 |
| Therapist visit, fasciectomy | 39.88 | 37.77 |
| Nurse visit, CCH or fasciectomy | 43.51 | 37.77 |

CCH, collagenase clostridium histolyticum; USD, United States dollars

*Include average salary, social security contributions, vacation pay, sick pay, overhead costs, and the degree of capacity utilization.

†Include costs of surgical and other materials, injections, premises, etc.

Price of 1 CCH injection = 970.19 USD.

**Table 3.** Number of visits to medical personnel, actual costs and outcomes of treating Dupuytren's contracture with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | CCH injection | Fasciectomy |
|---|---|---|
| Mean, median (IQR) number of visits to: | | |
| Doctor | 3* | 2* |
| Nurse | 0.33* | 3.0, 3.0 (2.0-3.8) |
| Therapist | 3* | 5.1, 4.0 (3.0-6.8) |
| Total cost per patient (USD) | 1418.04 | 2102.56 |
| Total cost per patient when 20% require 2 injections (USD) | 1675.24 | 2102.56 |
| Total extension deficit (degrees)† | | |
| mean (SD) | 20 (25) | 19 (19) |
| median (IQR) | 10 (0-30) | 10 (0-34) |

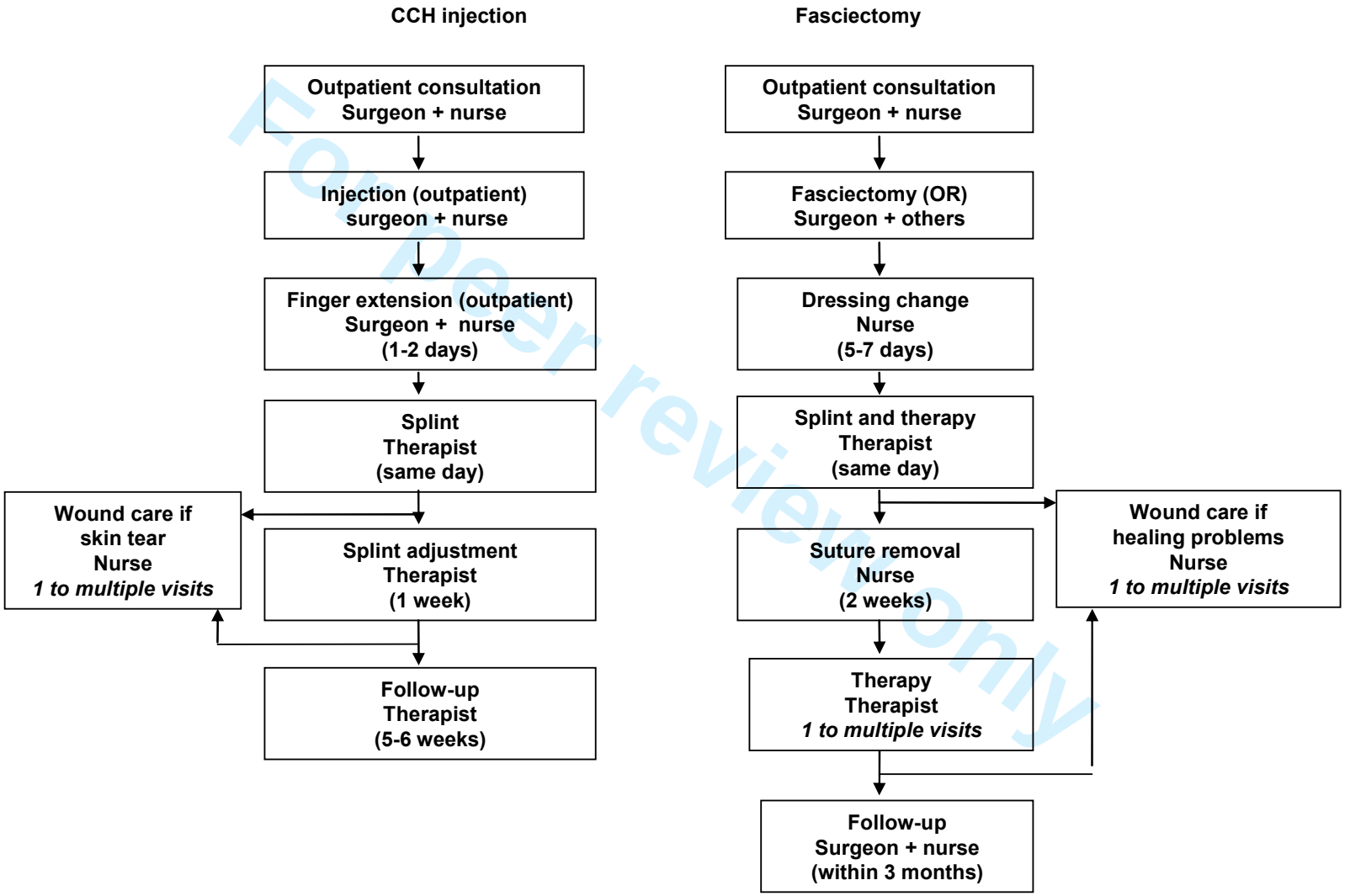
CCH, collagenase clostridium histolyticum; IQR, inter-quartile range; USD, United States dollars

* Number of visits to a doctor in both groups and to a therapist in the CCH group was similar for all patients (Figure 1); a third of CCH patients assumed to require 1 visit to a nurse.

†Metacarpophalangeal plus proximal interphalangeal joints

**Figure legend**

**Figure 1.** Diagram showing the various stages of treating patients with Dupuytren's contracture with collagenase clostridium histolyticum (CCH) injection or with fasciectomy as a day-surgery procedure performed in the operating room (OR). The number of visits is 1 unless specified otherwise.



STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** P 1+2 | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** | | |
| Background/rationale P 4-5 | 2 | Explain the scientific background and rationale for the investigation being reported |
| Objectives P 5 | 3 | State specific objectives, including any prespecified hypotheses |
| **Methods** | | |
| Study design P 6 | 4 | Present key elements of study design early in the paper |
| Setting P 6 | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants P 6 | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case |
| Variables P 8-10 | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/ measurement P 7-10 | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias P 10-11 | 9 | Describe any efforts to address potential sources of bias |
| Study size P 10 | 10 | Explain how the study size was arrived at |
| Quantitative variables P 10-11 | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods P 10-11 | 12 | (*a*) Describe all statistical methods, including those used to control for confounding |
| | | (*b*) Describe any methods used to examine subgroups and interactions |
| | | (*c*) Explain how missing data were addressed |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed<br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy |
| | | (*e*) Describe any sensitivity analyses |

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| **Results** | | |
| Participants<br>**P 12**<br>**Figure 1** | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| | | (b) Give reasons for non-participation at each stage |
| | | (c) Consider use of a flow diagram |
| Descriptive data<br>**P 12, Table 1** | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) |
| Outcome data<br>**P 12-13**<br>**Table 2 & 3** | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures |
| Main results<br>**P 12-13**<br>**Table 2 & 3** | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (*b*) Report category boundaries when continuous variables were categorized |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Other analyses<br>**P 12-13** | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | | |
| Key results<br>**P 14** | 18 | Summarise key results with reference to study objectives |
| Limitations<br>**P 15-16** | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Interpretation<br>**P 15-16** | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalisability<br>**P 15** | 21 | Discuss the generalisability (external validity) of the study results |
| **Other information** | | |
| Funding<br>**P 17** | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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# Costs of collagenase injections compared with fasciectomy in the treatment of Dupuytren's contracture: A retrospective cohort study

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# Costs for collagenase injections compared with fasciectomy in the treatment of Dupuytren's contracture: A retrospective cohort study

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## Abstract

**Objectives**: To compare collagenase injections and surgery (fasciectomy) for Dupuytren's contracture (DC) regarding actual total direct treatment costs and short-term outcomes.

**Design:** Retrospective cohort study

**Setting**: Orthopaedic department of a regional hospital in Sweden.

**Participants**: Patients aged 65 years or older with previously untreated DC of 30 degrees or greater in the metacarpophalangeal (MCP) and/or proximal interphalangeal (PIP) joints of the small, ring or middle finger. The collagenase group comprised 16 consecutive patients treated during the first 6 months following the introduction of collagenase as treatment for DC at the study centre. The controls were 16 patients randomly selected among those operated on with fasciectomy at the same centre during the preceding 3 years.

**Interventions**: Treatment with collagenase was given during two standard outpatient clinic visits (injection of 0.9 mg, distributed at multiple sites in a palpable cord, and next-day finger extension under local anaesthesia) followed by night-time splinting. Fasciectomy was done in the operating room (day surgery) under general or regional anaesthesia using standard technique, followed by therapy and splinting.

**Primary and secondary outcome measures**: Actual total direct costs (salaries of all medical personnel involved in care, medications, materials and other relevant costs), and total MCP and PIP extension deficit (degrees) measured by hand therapists at 6-12 weeks after treatment.

**Results**: Collagenase injection required fewer hospital outpatient visits to a therapist and nurse than fasciectomy. Total treatment cost for collagenase injection was 1418.04 USD and for fasciectomy 2102.56 USD. The post-treatment median (interquartile range) total extension deficit was 10 (0-30) for the collagenase group and 10 (0-34) for the fasciectomy group.

**Conclusions**: Treatment of Dupuytren's contracture with one collagenase injection costs 33% less than fasciectomy with equivalent efficacy at 6 weeks regarding reduction in contracture.

**Strengths and limitations of this study**

- This study presents previously unknown estimates of the actual costs of treating Dupuytren's contracture with Collagenase injections or fasciectomy
- Comparison of the actual costs of the two treatments are based on detailed definition and measurement of all relevant costs
- Outcomes of injections were prospectively measured but outcomes of surgery were based on medical records
- Costs may vary across countries
- Only short-term outcomes (6 weeks) were compared

## INTRODUCTION

Dupuytren's contracture (DC) is a common hand disorder causing finger contractures that may compromise hand function. Surgery in the form of limited fasciectomy has been the main treatment option for reducing the contracture.[1] In Sweden (population 9.5 millions), more than 3000 fasciectomy procedures are performed annually;[2] the actual number is probably higher because procedures performed by surgeons in private practice, although constituting a small proportion,[3] may not always be reported to the national database. Surgery is usually done in the main operating room under general or regional anaesthesia and the operating time is on average about 1 hour,[4] but can be substantially longer when severe contractures are present in multiple fingers. After surgery many patients require therapy and splints. Although surgery is often effective in reducing the contracture, postoperative complications such as nerve injury and wound healing problems are common and patients may develop contracture recurrence.[5,6]

Recently, injection with collagenase clostridium histolyticum (CCH) has been introduced as the first pharmacological treatment for DC after it was shown in a randomized controlled trial to be more effective than placebo injections in reducing contractures.[7] The treatment is a relatively simple procedure given in the outpatient clinic and rarely requires prolonged therapy. The current price of a CCH injection (in Sweden) is almost one thousand US dollars (USD) and one injection is used for each finger involved (unless contractures in 2 fingers are caused by a common cord). Because of economic pressure to control health care expenditures, the cost-effectiveness of surgical procedures has gained increased significance in hospital decision making. The cost analysis of different treatment procedures such as fasciectomy and

injection is therefore essential and the differences in short-term costs associated with these two techniques are important to consider.

To our knowledge no previous study has compared the actual costs of CCH injections with those of fasciectomy. One study based on a cost-utility analysis model concluded that open partial fasciectomy did not meet the cost-effectiveness threshold and that CCH injections would be cost-effective when priced below 945 USD.[8] Studies concerning costs of surgery have usually used reimbursement as a measure of costs,[9] but reimbursement does not necessarily reflect the actual cost of a procedure. Reimbursement levels for a certain procedure may vary substantially across and even within countries. For cost comparison of CCH injections and fasciectomy in DC the actual cost of each procedure is therefore a more relevant measure. When comparing the costs of two treatment methods, the outcome of the treatments must also be taken into consideration. However, we could not find studies that have compared the outcomes of CCH and fasciectomy.

The main aim of this retrospective cohort study was to compare CCH injections with fasciectomy regarding the actual total direct treatment costs. The secondary aim was to compare the short-term outcomes of these two treatment methods.

## PATIENTS AND METHODS

### Study participants

We conducted a retrospective cohort study at one orthopaedic department (Hässleholm, Kristianstad and Ystad Hospitals) in southern Sweden. The department is the only centre that treats patients with DC in a region with approximately 300,000 inhabitants.

Data on CCH injections were collected prospectively starting September 2011 when CCH was introduced as the main treatment option for DC at the department. The indication for treatment with CCH injections was identical to that previously used for surgery at the study centre, namely a palpable cord and contracture of 30 degrees or greater in the metacarpophalangeal (MCP) and/or proximal interphalangeal (PIP) joints. For this study we included the first 16 consecutive patients, aged 65 years or older, treated with CCH injections during the first 6 months (September 2011 through February 2012). We restricted the study to patients of non-working age because we aimed to compare only direct costs.

Data on fasciectomy were extracted from the medical records of patients treated at the department before the introduction of CCH injections. The patients were chosen among those aged 65 years or older, operated on with fasciectomy January 2009 through June 2011. Patients with surgery on more than 2 fingers, previous surgery for DC in the same hand, and additional procedures performed (e.g. skin graft or amputation) were excluded. A total of 113 patients were potentially eligible. Of these, a random sample of 15% was chosen by computer (statistical software), yielding 18 patients; 2 were excluded (1 had surgery for DC in the thumb and 1 chose to have postoperative therapy at another location). Thus, the fasciectomy group included 16 patients.

**Treatment and follow-up procedures**

Both treatments required an initial standard outpatient consultation visit to a hand surgeon or an orthopaedic surgeon, usually as a referral from the patient's general practitioner. Each surgeon was assisted by a nurse at the outpatient clinic. During the visit the treatment decision was made and the patient was scheduled for treatment (Fig 1).

***Collagenase injection***: Treatment with CCH required two standard outpatient visits to a hand surgeon: injection and next-day finger extension.[7] During these visits the surgeon was assisted by a nurse (all treatments were given by the same hand surgeon). A modified injection method was used for all treated fingers; after reconstituting CCH with 0.39 ml of diluent, according to the standard procedure, all the reconstituted CCH (0.9 mg) was injected into the cord, distributed at multiple sites. The following day, finger manipulation (extension) was done under local anaesthesia. Immediately after finger extension the patient went to the therapist and received a splint for use at night for 8 weeks. A second visit to the therapist was done 1 week post-injection for splint adjustment and therapy instructions. Patients who during finger extension developed a skin tear that was judged to require dressing change were asked to visit a nurse within 2 to 3 days. Further visits to the nurse were done when necessary, depending on wound status. No routine post-treatment visits were scheduled to the treating surgeon and the final follow-up (usually at 5-6 weeks) was done by the therapist. If the patient was not satisfied with the degree of correction after the first injection, the therapist arranged a consultation to the treating surgeon for consideration of further treatment.

***Fasciectomy***: Fasciectomy was done as a day-surgery procedure in the main operating room (OR). The surgery was done by one of six different surgeons (three experienced hand surgeons and three orthopaedic surgeons with experience in hand surgery) using standard

technique for limited open fasciectomy.[10] General anaesthesia or axillary block was used. According to routine procedures at the hospital general anaesthesia was administered by a nurse anaesthetist and axillary block was administered by an anaesthesiologist, after which the nurse anaesthetist was in charge of the patient's care with anaesthesiologist help obtained when needed. The surgery was done by a surgeon (no assistant) with a team consisting of an OR nurse, a nurse anaesthetist and 2 nurse assistants (1 participated only in the initial preparations). The electronic records for each surgical procedure include the exact start and finish times for the preparations before surgery, anaesthesia, the actual surgery (i.e. operating time from incision to dressing), and the work done after the surgeon has completed the operation and until the patient is taken back to the recovery room. After returning from the OR the patient stayed in the recovery room until discharge from the day-surgery unit. The time of discharge is documented in the electronic records. Thus, for each patient 3 times were recorded; the operating time, the total OR time (from start of preparations until room ready for next procedure), and the time at the recovery room until discharge.

After fasciectomy all patients visited a nurse for dressing change after 5 to 7 days, followed immediately by a visit to a therapist for a splint and therapy instructions. A second visit to the nurse for wound inspection and suture removal was done at approximately 2 weeks. Further visits to the nurse were done when necessary, depending on wound status. Patients also had further visits to the therapist for scar management, splint adjustments and therapy instructions as required. The treating therapist decided on the frequency and duration of therapy. Patients had 1 postoperative follow-up visit to the surgeon timed according to surgeon preference.

**Cost measurement**

A detailed analysis of the salaries of physicians and non-physician medical personnel involved in the treatment of patients with DC was performed for CCH injection and fasciectomy. We identified the average salaries of individuals and used the average time units to calculate the cost of manpower. The costs of all materials, premises and other costs were calculated. We included fixed assets such as the costs of the premises and its expenses and the costs of surgical equipment. All costs were measured based on 2011 salaries/prices. These costs include; salaries of all medical personnel involved in the direct care of the patients including social security contributions, vacation pay and sick pay (averaged for each category: specialist orthopaedic surgeon, anaesthesiologist, nurse, nurse assistant and therapist), hospital overhead costs, the degree of capacity utilization, medications, surgical and other material, premises and other costs. The average salaries were based on all respective medical personnel group in the public health care sector in the region. We did not include costs of non-medical personnel involved in the care (such as receptionists, secretaries, cleaners, etc).

A standard outpatient visit to a doctor was 20 minutes. For the 2 CCH visits (injection and finger extension) we used the standard time for the surgeon and 25 minutes for the assisting nurse (to account for the time needed for preparations and work after the session had ended). For fasciectomy we used the mean operating time, total OR time and recovery time, according to the personnel involved and adjusted as required. For the operating surgeon we used the mean operating time plus 25 minutes needed for additional work (assessing the patient and marking the surgical site before surgery, scrubbing, writing the surgical notes and discharging the patient after surgery). For the non-physician personnel we used the mean total operating room time and for the anaesthesiologist we used half that time (one anaesthesiologist is usually assigned to 2 operating rooms simultaneously and the care of these patients after

surgery). For recovery room personnel (a nurse and a nurse assistant are in charge of up to 5 patients simultaneously), we used a fifth of the recovery time plus 5 minutes (preoperative preparations). A standard outpatient visit to a nurse (for wound care after CCH injection or fasciectomy) was 45 minutes. A standard visit to therapist after CCH injection was 30 minutes and after fasciectomy 45 minutes. For each patient the exact number of hospital outpatient visits to a doctor, nurse or therapist, related to the treatments, was retrieved from the Patient Administrative System.

**Outcome measurement**

At baseline and at all follow-up visits range of motion including extension and flexion of the MCP and PIP joints of the fingers was measured with a goniometer. In the fasciectomy group the baseline measurements were done by the surgeons during the visit that resulted in the patient being scheduled for fasciectomy and the post-treatment measurements were done by six different therapists; these measurements were recorded in the patient's electronic medical records. In the CCH group all measurements (immediately before injection and at follow-up) were done by the same therapist, as part of a research project. The measurements recorded at baseline and at the final visit were used in the analysis.

**Analysis**

In 2 previous randomized trials the proportion of MCP joints that were reduced to 0 to 5 degrees of extension deficit was 45% at 30 days after first CCH injection[7] and 94% at 6 weeks after fasciectomy.[11] To detect a difference of this magnitude between the 2 groups (80% power and 0.05 significance level) would require a sample of 13 patients in each group. The cost estimation of CCH was based on standard procedures independent of sample size. For the cost of fasciectomy, a random sample of 15% from 113 fasciectomy-treated patients

was judged adequate to provide representative average procedure time estimates and number of visits to medical personnel, on which the total cost was based. Data are shown as mean and SD and/or median and interquartile range (IQR). We calculated the average total cost of treatment per patient when only 1 CCH injection is given. We also calculated the cost if 20% of the patients would need 2 CCH injections given on separate sessions to obtain satisfactory contracture reduction. Because some patients who developed skin tears during finger extension chose to have dressing change, when necessary, at home or at primary care, only 1 nurse visit was recorded in the Patient Administrative System. We therefore made the calculations assuming 1 of 3 patients in the CCH group would require 1 nurse visit. We also conducted a sensitivity analysis with the conservative assumption of 1 nurse visit per patient. All costs were calculated in Swedish Kronor (SEK) and converted to USD using the rate of 1 USD = 6.676 SEK (Sweden's Central Bank average for 2011). The within-group change in extension deficit was analyzed with the Wilcoxon test. We also compared the 2 groups with regard to improvement in total extension deficit using the Mann-Whitney test. A p value below 0.05 was used to indicate statistical significance.

# RESULTS

The 16 patients in the CCH group and the 16 patients in the fasciectomy group had similar characteristics (Table 1). In the fasciectomy group half of the patients received general anaesthesia and the other half axillary block. The mean operating time was 62 (SD 27) minutes, mean total OR time 138 (SD 43) minutes, and mean postoperative time spent at the day-surgery recovery room until discharge 215 (SD 41) minutes. The median time from surgery to end of therapy was 6.3 weeks (IQR 4.0-11.5) and to the postoperative follow-up by the surgeon 7.5 weeks (IQR 6.0-12.0). None of the patients in the CCH group required further therapy than the standard visits. Of the 16 patients, 9 developed skin tears ranging from minor superficial skin breakage that did not require further wound care to deeper wound that required 1 or more dressing changes. All wounds had healed within 2 weeks after injection.

## Costs

The cost specifications for the two treatments are shown in Table 2. The largest treatment cost for CCH injections was the cost of the injection itself (970.19 USD) and for fasciectomy the cost of personnel (783.97 USD) and other costs (380.81 USD) associated with the surgery in the operating room. Compared to fasciectomy, treatment with CCH injections required fewer outpatient hospital visits to a nurse and a therapist (Table 3).

The total treatment cost with 1 CCH injection was 33% lower than that for fasciectomy (1418.04 versus 2102.56 USD). The cost was still lower (1675.24 USD) if 20% of patients treated with CCH would require 2 injections in the same hand, given in separate sessions. In the sensitivity analysis the cost of CCH injections assuming an average of 1 nurse visit per

patient was 1472.51 USD when 1 injection is given and 1696.79 USD when 20% would require 2 injections.

**Outcomes**

Of the 16 patients in the CCH and fasciectomy groups, 7 and 9 patients respectively achieved an extension deficit of 0 to 5 degrees in the joint with the largest extension deficit. In both groups the improvement in total extension deficit was statistically significant ($p < 0.001$) and the extension deficits after CCH and fasciectomy were similar (median 10 degrees) (Table 3). The median improvement in total extension deficit in the CCH group was 65 (IQR 56-81) degrees and in the fasciectomy group 50 (IQR 41-60) degrees ($p=0.007$).

No complications were observed in any of the groups at the final follow-up.

## DISCUSSION

Our study shows that treatment of DC with a single collagenase injection is associated with lower costs than surgery (fasciectomy) and the short-term outcomes (6 weeks) regarding reduction in finger joint contractures are similar. The costs are still lower when assuming that 20% of the patients would require 2 injections in the same hand, but if more than 5 of 10 patients need 2 injections the costs would exceed those of fasciectomy. Our estimates of the costs assuming 20% would require 2 injections were based on separate treatment sessions; the costs would be even lower if the 2 injections are given in the same session, which would probably become the usual practice.[12] Further, our results should be considered conservative since we have not considered complications (such as wound infection and chronic regional pain syndrome) that are probably more frequent after surgery than after CCH injections and would therefore add to the total costs. The study by Hurst et al.[7] reported use of an average of about 2 CCH injections per patient. However, in that study finger extension, which often is a painful procedure, was done without anaesthesia, which may have reduced the degree of initial contracture correction and thus necessitating a second injection. As in our study, use of local anaesthesia is currently the standard procedure. In addition, Hurst et al. injected 0.58 mg CCH into one part of the cord whereas our technique is to inject the whole content of a single CCH injection (0.9 mg) into the cord at multiple sites, which would probably increase the efficacy of a single injection.

For fasciectomy, the largest cost was represented by the various costs associated with a day-surgery procedure of approximately 1 hour duration in the operating room. The cost would be lower if the average operating time were shorter than our estimate of 62 minutes. In a recent study of DC in 12 European countries (based on a surgeon survey and patient chart review),

the mean operating time for fasciectomy across all countries was 67 minutes (Nordic 63, Eastern 69, Western 66, and Mediterranean 68 minutes).[4] A potential advantage with CCH injections is the possibility to treat patients with bilateral disease in 1 stage, which is uncommon with surgery considering the nature of the procedure. In contrast, patients with contractures involving 3 or more fingers can be treated with surgery in one session, but would need at least 2 CCH injections and, in more severe cases, 2 or more treatment sessions.

Skin tears ranging from minor superficial skin breakage to deeper wounds occurred in more than half the patients after CCH injections in our study. Skin tears following CCH injections were reported in 11% in the multicenter randomized trial,[7] and in up to 19% in other studies.[13,14] Skin tears are more likely to occur in severe contractures especially of the small finger.[9] Because the incidence and severity of skin tears (ie, need for wound care) may vary we calculated the costs assuming that, on average, one third of the patients would require 1 nurse visit and also did a sensitivity analysis assuming an average of 1 nurse visit. We believe these estimates cover the costs of wound care even if the true incidence of skin tears is higher than previously reported.

We only compared direct costs, and therefore did not include costs of lost productivity or sick leave. Among employed patients, sick leave is more likely to be necessary and longer after fasciectomy than after CCH injections. According to the Swedish Social Insurance Agency the total cost of a 1-week sick leave based on the average salary in Sweden 2011 (including sick-pay, general payroll tax, vacation-pay and overhead costs) exceeds 1300 USD (www.scb.se). In addition, the direct costs of CCH injections and fasciectomy may differ across countries and settings. In a Canadian study that estimated the cost (during 2005) of open carpal tunnel release, a 10-minute procedure done under local anaesthesia, the total cost

(excluding surgeon's fee) was 137 CAD when done in the main operating room and 53 CAD dollars when done in the office.[15] Although the largest treatment cost for CCH injections was the cost of the injection itself, which may be substantially higher in some countries, the costs of surgery in these countries may also be higher. In a study involving 24 patients treated with fasciectomy at a single US hospital from 2008 to 2010 the average direct cost, defined as costs billed from hospital charges (facility fees) and professional charges (surgeon and anaesthesia fees) was estimated to be 11,240 USD.[9]

A limitation of our study is that only very short-term outcomes were measured. The improvement was high and the minor residual contracture was similar for CCH and fasciectomy. Differences in long-term outcomes may change the cost-effectiveness of these treatments because if they differ substantially in the recurrence rate and the need for further treatments the cost of subsequent treatments should also be considered. According to the most recent published data regarding recurrence after CCH injections (defined as contracture increase of 20 degrees or greater in the presence of a palpable cord in joints initially corrected to a maximum of 5-degree contracture), the overall rate in 623 joints at 3 years was 35% (MCP 27% and PIP 56%) but the recurrence required treatment in only 7%.[16] Following fasciectomy a 3-year recurrence rate of 12% has been reported in two studies; in the first study, 4 of 33 hands had more than 30 degrees increase in joint contracture compared to 6 weeks,[11]and in the second study, 11 of 90 fingers showed progressive recurrence of PIP joint contracture but no specific definition of recurrence was stated.[17] Thus, depending on the proportion of patients that subsequently need repeated treatment because of recurrent contracture in the treated fingers it is possible that in the long-term the direct costs of treatment with CCH may exceed those of fasciectomy.

Another limitation is that in the fasciectomy group the baseline range-of-motion measurements were done by different surgeons and the follow-up measurements by different therapists. The inter-observer reliability of these measurements is unknown and there might be a risk that the surgeon overestimated the preoperative contracture and the treating therapist underestimated residual contracture. However, we do not believe this issue has a substantial influence because fasciectomy was the only treatment option and the results of the post-treatment measurements, done by therapists, were similar in both groups.

In conclusion, treatment of DC with a single CCH injection costs 33% less, in direct costs, than fasciectomy with equivalent short-term efficacy (6 weeks) regarding reduction in contracture.

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**Contributorship Statement**

IA, ES, AL: Study conception and design, acquisition of data, analysis and interpretation of data, and drafting of the article.

EA: Acquisition of data, and critical revision of the article for important intellectual content.

MW: Analysis and interpretation of data and critical revision of the article for important intellectual content.

All authors approved the final submitted version.

**Competing Interests**

Dr. Atroshi was a member of an Expert Group on Dupuytren's disease for Pfizer 2012. The other authors have no competing interests.

**Data Sharing Statement**

**Data are available on request from Dr. Atroshi**

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**Table 1** Characteristics of the two samples of patients with Dupuytren's contracture treated with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | | CCH injection | Fasciectomy |
|---|---|---|---|
| Number of patients (men) | | 16 (11) | 16 (13) |
| Age (yrs), mean (SD) | | 69 (4) | 71 (5) |
| Number of fingers treated* | | | |
| Small | | 11 | 9 |
| Ring | | 7 | 8 |
| Middle | | 0 | 1 |
| Extension deficit (degrees) | | | |
| Total† | mean (SD) | 90 (39) | 71 (28) |
| | median (IQR) | 70 (60-115) | 75 (45-89) |
| MCP‡ | mean (SD) | 64 (16) | 60 (17) |
| | median (IQR) | 65 (60-75) | 60 (41-80) |
| PIP‡ | mean (SD) | 55 (22) | 46 (18) |
| | median (IQR) | 55 (43-70) | 40 (35-48) |

CCH, collagenase clostridium histolyticum; IQR, interquartile range

*2 patients in each group had 2 fingers treated.

† Metacarpophalangeal (MCP) plus proximal interphalangeal (PIP) joints in all treated fingers (in patients with 2 fingers treated the finger with largest extension deficit was used).

‡ The values showing MCP and PIP extension deficits separately include only joints with contracture (no MCP contracture in 1 patient in the CCH group and 2 patients in the fasciectomy group and no PIP contracture in 7 patients in each group).

**Table 2** Cost specification for the various stages of treating Dupuytren's contracture with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | Personnel costs* (USD) | Other costs† (USD) |
|---|---|---|
| Doctor visit, CCH or fasciectomy (doctor and nurse) | 65.80 | 16.78 |
| Injection, CCH (doctor and nurse) | 70.63 | 991.16 |
| Finger extension, CCH (doctor and nurse) | 70.63 | 20.97 |
| Therapist visit, CCH | 26.58 | 25.16 |
| Surgery, fasciectomy (doctors and others) | 783.97 | 380.81 |
| Day surgery care, fasciectomy | 88.10 | 52.41 |
| Therapist visit, fasciectomy | 39.88 | 37.77 |
| Nurse visit, CCH or fasciectomy | 43.51 | 37.77 |

CCH, collagenase clostridium histolyticum; USD, United States dollars

*Include average salary, social security contributions, vacation pay, sick pay, overhead costs, and the degree of capacity utilization.

†Include costs of surgical and other materials, injections, premises, etc.

Price of 1 CCH injection = 970.19 USD.

**Table 3** Number of visits to medical personnel, actual costs and short-term outcomes of treating Dupuytren's contracture with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | | CCH injection | Fasciectomy |
|---|---|---|---|
| Mean, median (IQR) number of visits to: | | | |
| Doctor | | 3* | 2* |
| Nurse | | 0.33* | 3.0, 3.0 (2.0-3.8) |
| Therapist | | 3* | 5.1, 4.0 (3.0-6.8) |
| Total cost per patient (USD) | | 1418.04 | 2102.56 |
| Total cost per patient when 20% require 2 injections (USD) | | 1675.24 | 2102.56 |
| Extension deficit (degrees)† | | | |
| Total | mean (SD) | 20 (25) | 19 (19) |
| | median (IQR) | 10 (0-30) | 10 (0-34) |
| MCP | mean (SD) | 10 (17) | 8 (10) |
| | median (IQR) | 0 (0-15) | 0 (0-20) |
| PIP | mean (SD) | 23 (18) | 21 (13) |
| | median (IQR) | 20 (8-35) | 25 (8-33) |

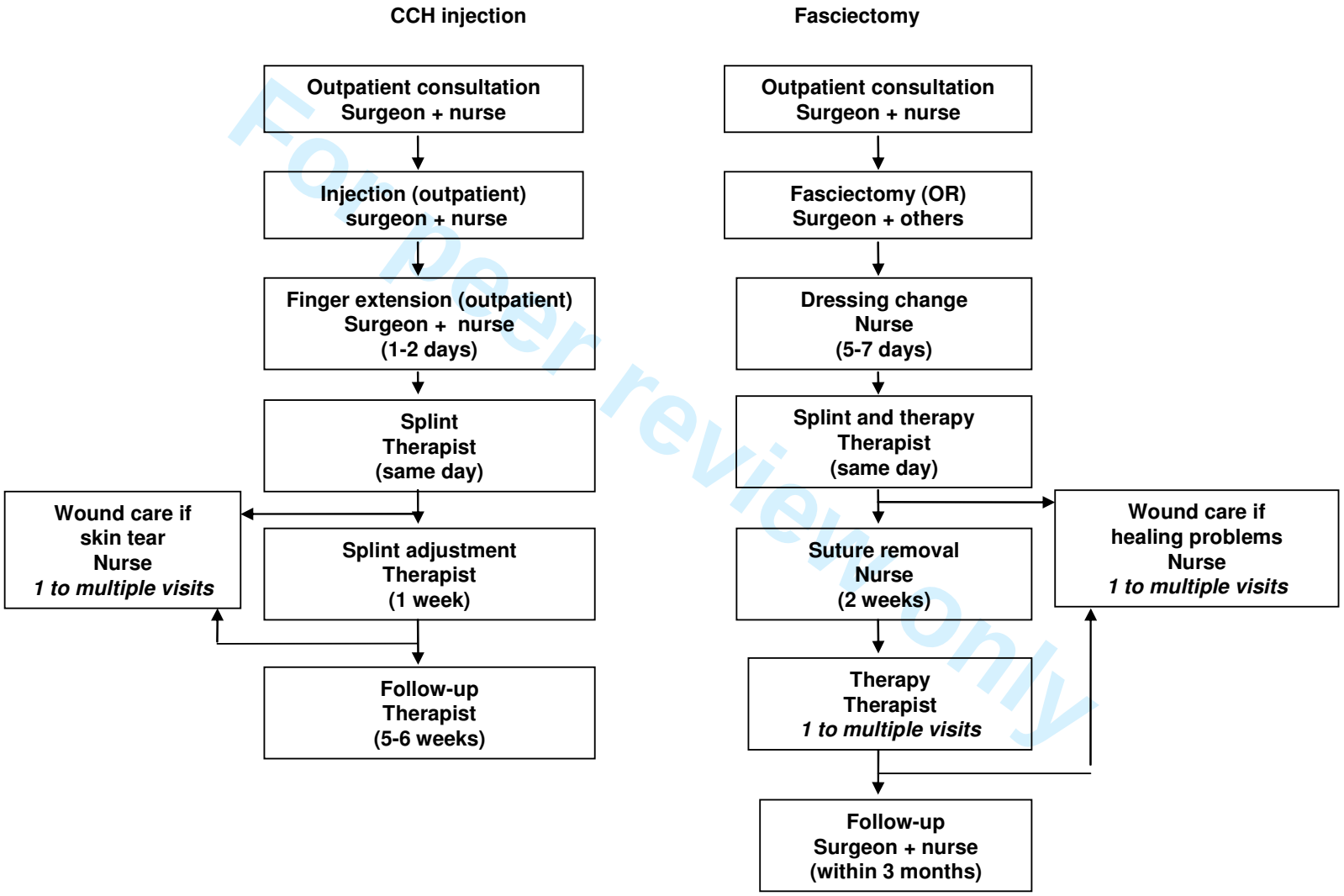
CCH, collagenase clostridium histolyticum; IQR, interquartile range; USD, United States dollars

* Number of visits to a doctor in both groups and to a therapist in the CCH group was similar for all patients (Figure 1); a third of CCH patients assumed to require 1 visit to a nurse.

† Metacarpophalangeal (MCP) plus proximal interphalangeal (PIP) joints in all treated fingers. The values showing MCP and PIP extension deficits separately include only joints with pretreatment contracture (see footnote in Table 1).

**Figure legend**

**Figure 1.** Diagram showing the various stages of treating patients with Dupuytren's contracture with collagenase clostridium histolyticum (CCH) injection or with fasciectomy as a day-surgery procedure performed in the operating room (OR). The number of visits is 1 unless specified otherwise.



# Costs for collagenase injections compared with fasciectomy in the treatment of Dupuytren's contracture: A retrospective cohort study

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## Abstract

**Objectives**: To compare collagenase injections and surgery (fasciectomy) for Dupuytren's contracture (DC) regarding actual total direct treatment costs and short-term outcomes.

**Design:** Retrospective cohort study

**Setting**: Orthopaedic department of a regional hospital in Sweden.

**Participants**: Patients aged 65 years or older with previously untreated DC of 30 degrees or greater in the metacarpophalangeal (MCP) and/or proximal interphalangeal (PIP) joints of the small, ring or middle finger. The collagenase group comprised 16 consecutive patients treated during the first 6 months following the introduction of collagenase as treatment for DC at the study centre. The controls were 16 patients randomly selected among those operated on with fasciectomy at the same centre during the preceding 3 years.

**Interventions**: Treatment with collagenase was given during two standard outpatient clinic visits (injection of 0.9 mg, distributed at multiple sites in a palpable cord, and next-day finger extension under local anaesthesia) followed by night-time splinting. Fasciectomy was done in the operating room (day surgery) under general or regional anaesthesia using standard technique, followed by therapy and splinting.

**Primary and secondary outcome measures**: Actual total direct costs (salaries of all medical personnel involved in care, medications, materials and other relevant costs), and total MCP and PIP extension deficit (degrees) measured by hand therapists at 6-12 weeks after treatment.

**Results**: Collagenase injection required fewer hospital outpatient visits to a therapist and nurse than fasciectomy. Total treatment cost for collagenase injection was 1418.04 USD and for fasciectomy 2102.56 USD. The post-treatment median (interquartile range) total extension deficit was 10 (0-30) for the collagenase group and 10 (0-34) for the fasciectomy group.

**Conclusions**: Treatment of Dupuytren's contracture with one collagenase injection costs 33% less than fasciectomy with equivalent efficacy at 6 weeks regarding reduction in contracture.

**Strengths and limitations of this study**

- This study presents previously unknown estimates of the actual costs of treating Dupuytren's contracture with Collagenase injections or fasciectomy
- Comparison of the actual costs of the two treatments are based on detailed definition and measurement of all relevant costs
- Outcomes of injections were prospectively measured but outcomes of surgery were based on medical records
- Costs may vary across countries
- Only short-term outcomes (6 weeks) were compared

## INTRODUCTION

Dupuytren's contracture (DC) is a common hand disorder causing finger contractures that may compromise hand function. Surgery in the form of limited fasciectomy has been the main treatment option for reducing the contracture.[1] In Sweden (population 9.5 millions), more than 3000 fasciectomy procedures are performed annually;[2] the actual number is probably higher because procedures performed by surgeons in private practice, although constituting a small proportion,[3] may not always be reported to the national database. Surgery is usually done in the main operating room under general or regional anaesthesia and the operating time is on average about 1 hour,[4] but can be substantially longer when severe contractures are present in multiple fingers. After surgery many patients require therapy and splints. Although surgery is often effective in reducing the contracture, postoperative complications such as nerve injury and wound healing problems are common and patients may develop contracture recurrence.[5,6]

Recently, injection with collagenase clostridium histolyticum (CCH) has been introduced as the first pharmacological treatment for DC after it was shown in a randomized controlled trial to be more effective than placebo injections in reducing contractures.[7] The treatment is a relatively simple procedure given in the outpatient clinic and rarely requires prolonged therapy. The current price of a CCH injection (in Sweden) is almost one thousand US dollars (USD) and one injection is used for each finger involved (unless contractures in 2 fingers are caused by a common cord). Because of economic pressure to control health care expenditures, the cost-effectiveness of surgical procedures has gained increased significance in hospital decision making. The cost analysis of different treatment procedures such as fasciectomy and

injection is therefore essential and the differences in short-term costs associated with these two techniques are important to consider.

To our knowledge no previous study has compared the actual costs of CCH injections with those of fasciectomy. One study based on a cost-utility analysis model concluded that open partial fasciectomy did not meet the cost-effectiveness threshold and that CCH injections would be cost-effective when priced below 945 USD.[8] Studies concerning costs of surgery have usually used reimbursement as a measure of costs,[9] but reimbursement does not necessarily reflect the actual cost of a procedure. Reimbursement levels for a certain procedure may vary substantially across and even within countries. For cost comparison of CCH injections and fasciectomy in DC the actual cost of each procedure is therefore a more relevant measure. When comparing the costs of two treatment methods, the outcome of the treatments must also be taken into consideration. However, we could not find studies that have compared the outcomes of CCH and fasciectomy.

The main aim of this retrospective cohort study was to compare CCH injections with fasciectomy regarding the actual total direct treatment costs. The secondary aim was to compare the short-term outcomes of these two treatment methods.

## PATIENTS AND METHODS

### Study participants

We conducted a retrospective cohort study at one orthopaedic department (Hässleholm, Kristianstad and Ystad Hospitals) in southern Sweden. The department is the only centre that treats patients with DC in a region with approximately 300,000 inhabitants.

Data on CCH injections were collected prospectively starting September 2011 when CCH was introduced as the main treatment option for DC at the department. The indication for treatment with CCH injections was identical to that previously used for surgery at the study centre, namely a palpable cord and contracture of 30 degrees or greater in the metacarpophalangeal (MCP) and/or proximal interphalangeal (PIP) joints. For this study we included the first 16 consecutive patients, aged 65 years or older, treated with CCH injections during the first 6 months (September 2011 through February 2012). We restricted the study to patients of non-working age because we aimed to compare only direct costs.

Data on fasciectomy were extracted from the medical records of patients treated at the department before the introduction of CCH injections. The patients were chosen among those aged 65 years or older, operated on with fasciectomy January 2009 through June 2011. Patients with surgery on more than 2 fingers, previous surgery for DC in the same hand, and additional procedures performed (e.g. skin graft or amputation) were excluded. A total of 113 patients were potentially eligible. Of these, a random sample of 15% was chosen by computer (statistical software), yielding 18 patients; 2 were excluded (1 had surgery for DC in the thumb and 1 chose to have postoperative therapy at another location). Thus, the fasciectomy group included 16 patients.

**Treatment and follow-up procedures**

Both treatments required an initial standard outpatient consultation visit to a hand surgeon or an orthopaedic surgeon, usually as a referral from the patient's general practitioner. Each surgeon was assisted by a nurse at the outpatient clinic. During the visit the treatment decision was made and the patient was scheduled for treatment (Fig 1).

***Collagenase injection***: Treatment with CCH required two standard outpatient visits to a hand surgeon: injection and next-day finger extension.[7] During these visits the surgeon was assisted by a nurse (all treatments were given by the same hand surgeon). A modified injection method was used for all treated fingers; after reconstituting CCH with 0.39 ml of diluent, according to the standard procedure, all the reconstituted CCH (0.9 mg) was injected into the cord, distributed at multiple sites. The following day, finger manipulation (extension) was done under local anaesthesia. Immediately after finger extension the patient went to the therapist and received a splint for use at night for 8 weeks. A second visit to the therapist was done 1 week post-injection for splint adjustment and therapy instructions. Patients who during finger extension developed a skin tear that was judged to require dressing change were asked to visit a nurse within 2 to 3 days. Further visits to the nurse were done when necessary, depending on wound status. No routine post-treatment visits were scheduled to the treating surgeon and the final follow-up (usually at 5-6 weeks) was done by the therapist. If the patient was not satisfied with the degree of correction after the first injection, the therapist arranged a consultation to the treating surgeon for consideration of further treatment.

***Fasciectomy***: Fasciectomy was done as a day-surgery procedure in the main operating room (OR). The surgery was done by one of six different surgeons (three experienced hand surgeons and three orthopaedic surgeons with experience in hand surgery) using standard

technique for limited open fasciectomy.[10] General anaesthesia or axillary block was used. According to routine procedures at the hospital general anaesthesia was administered by a nurse anaesthetist and axillary block was administered by an anaesthesiologist, after which the nurse anaesthetist was in charge of the patient's care with anaesthesiologist help obtained when needed. The surgery was done by a surgeon (no assistant) with a team consisting of an OR nurse, a nurse anaesthetist and 2 nurse assistants (1 participated only in the initial preparations). The electronic records for each surgical procedure include the exact start and finish times for the preparations before surgery, anaesthesia, the actual surgery (i.e. operating time from incision to dressing), and the work done after the surgeon has completed the operation and until the patient is taken back to the recovery room. After returning from the OR the patient stayed in the recovery room until discharge from the day-surgery unit. The time of discharge is documented in the electronic records. Thus, for each patient 3 times were recorded; the operating time, the total OR time (from start of preparations until room ready for next procedure), and the time at the recovery room until discharge.

After fasciectomy all patients visited a nurse for dressing change after 5 to 7 days, followed immediately by a visit to a therapist for a splint and therapy instructions. A second visit to the nurse for wound inspection and suture removal was done at approximately 2 weeks. Further visits to the nurse were done when necessary, depending on wound status. Patients also had further visits to the therapist for scar management, splint adjustments and therapy instructions as required. The treating therapist decided on the frequency and duration of therapy. Patients had 1 postoperative follow-up visit to the surgeon timed according to surgeon preference.

**Cost measurement**

A detailed analysis of the salaries of physicians and non-physician medical personnel involved in the treatment of patients with DC was performed for CCH injection and fasciectomy. We identified the average salaries of individuals and used the average time units to calculate the cost of manpower. The costs of all materials, premises and other costs were calculated. We included fixed assets such as the costs of the premises and its expenses and the costs of surgical equipment. All costs were measured based on 2011 salaries/prices. These costs include; salaries of all medical personnel involved in the direct care of the patients including social security contributions, vacation pay and sick pay (averaged for each category: specialist orthopaedic surgeon, anaesthesiologist, nurse, nurse assistant and therapist), hospital overhead costs, the degree of capacity utilization, medications, surgical and other material, premises and other costs. The average salaries were based on all respective medical personnel group in the public health care sector in the region. We did not include costs of non-medical personnel involved in the care (such as receptionists, secretaries, cleaners, etc).

A standard outpatient visit to a doctor was 20 minutes. For the 2 CCH visits (injection and finger extension) we used the standard time for the surgeon and 25 minutes for the assisting nurse (to account for the time needed for preparations and work after the session had ended). For fasciectomy we used the mean operating time, total OR time and recovery time, according to the personnel involved and adjusted as required. For the operating surgeon we used the mean operating time plus 25 minutes needed for additional work (assessing the patient and marking the surgical site before surgery, scrubbing, writing the surgical notes and discharging the patient after surgery). For the non-physician personnel we used the mean total operating room time and for the anaesthesiologist we used half that time (one anaesthesiologist is usually assigned to 2 operating rooms simultaneously and the care of these patients after

surgery). For recovery room personnel (a nurse and a nurse assistant are in charge of up to 5 patients simultaneously), we used a fifth of the recovery time plus 5 minutes (preoperative preparations). A standard outpatient visit to a nurse (for wound care after CCH injection or fasciectomy) was 45 minutes. A standard visit to therapist after CCH injection was 30 minutes and after fasciectomy 45 minutes. For each patient the exact number of hospital outpatient visits to a doctor, nurse or therapist, related to the treatments, was retrieved from the Patient Administrative System.

**Outcome measurement**

At baseline and at all follow-up visits range of motion including extension and flexion of the MCP and PIP joints of the fingers was measured with a goniometer. In the fasciectomy group the baseline measurements were done by the surgeons during the visit that resulted in the patient being scheduled for fasciectomy and the post-treatment measurements were done by six different therapists; these measurements were recorded in the patient's electronic medical records. In the CCH group all measurements (immediately before injection and at follow-up) were done by the same therapist, as part of a research project. The measurements recorded at baseline and at the final visit were used in the analysis.

**Analysis**

In 2 previous randomized trials the proportion of MCP joints that were reduced to 0 to 5 degrees of extension deficit was 45% at 30 days after first CCH injection[7] and 94% at 6 weeks after fasciectomy.[11] To detect a difference of this magnitude between the 2 groups (80% power and 0.05 significance level) would require a sample of 13 patients in each group. The cost estimation of CCH was based on standard procedures independent of sample size. For the cost of fasciectomy, a random sample of 15% from 113 fasciectomy-treated patients

was judged adequate to provide representative average procedure time estimates and number of visits to medical personnel, on which the total cost was based. Data are shown as mean and SD and/or median and interquartile range (IQR). We calculated the average total cost of treatment per patient when only 1 CCH injection is given. We also calculated the cost if 20% of the patients would need 2 CCH injections given on separate sessions to obtain satisfactory contracture reduction. Because some patients who developed skin tears during finger extension chose to have dressing change, when necessary, at home or at primary care, only 1 nurse visit was recorded in the Patient Administrative System. We therefore made the calculations assuming 1 of 3 patients in the CCH group would require 1 nurse visit. We also conducted a sensitivity analysis with the conservative assumption of 1 nurse visit per patient. All costs were calculated in Swedish Kronor (SEK) and converted to USD using the rate of 1 USD = 6.676 SEK (Sweden's Central Bank average for 2011). The within-group change in extension deficit was analyzed with the Wilcoxon test. We also compared the 2 groups with regard to improvement in total extension deficit using the Mann-Whitney test. A p value below 0.05 was used to indicate statistical significance.

## RESULTS

The 16 patients in the CCH group and the 16 patients in the fasciectomy group had similar characteristics (Table 1). In the fasciectomy group half of the patients received general anaesthesia and the other half axillary block. The mean operating time was 62 (SD 27) minutes, mean total OR time 138 (SD 43) minutes, and mean postoperative time spent at the day-surgery recovery room until discharge 215 (SD 41) minutes. The median time from surgery to end of therapy was 6.3 weeks (IQR 4.0-11.5) and to the postoperative follow-up by the surgeon 7.5 weeks (IQR 6.0-12.0). None of the patients in the CCH group required further therapy than the standard visits. Of the 16 patients, 9 developed skin tears ranging from minor superficial skin breakage that did not require further wound care to deeper wound that required 1 or more dressing changes. All wounds had healed within 2 weeks after injection.

### Costs

The cost specifications for the two treatments are shown in Table 2. The largest treatment cost for CCH injections was the cost of the injection itself (970.19 USD) and for fasciectomy the cost of personnel (783.97 USD) and other costs (380.81 USD) associated with the surgery in the operating room. Compared to fasciectomy, treatment with CCH injections required fewer outpatient hospital visits to a nurse and a therapist (Table 3).

The total treatment cost with 1 CCH injection was 33% lower than that for fasciectomy (1418.04 versus 2102.56 USD). The cost was still lower (1675.24 USD) if 20% of patients treated with CCH would require 2 injections in the same hand, given in separate sessions. In the sensitivity analysis the cost of CCH injections assuming an average of 1 nurse visit per

patient was 1472.51 USD when 1 injection is given and 1696.79 USD when 20% would require 2 injections.

**Outcomes**

Of the 16 patients in the CCH and fasciectomy groups, 7 and 9 patients respectively achieved an extension deficit of 0 to 5 degrees in the joint with the largest extension deficit. In both groups the improvement in total extension deficit was statistically significant ($p < 0.001$) and the extension deficits after CCH and fasciectomy were similar (median 10 degrees) (Table 3). The median improvement in total extension deficit in the CCH group was 65 (IQR 56-81) degrees and in the fasciectomy group 50 (IQR 41-60) degrees ($p=0.007$).

No complications were observed in any of the groups at the final follow-up.

## DISCUSSION

Our study shows that treatment of DC with a single collagenase injection is associated with lower costs than surgery (fasciectomy) and the short-term outcomes (6 weeks) regarding reduction in finger joint contractures are similar. The costs are still lower when assuming that 20% of the patients would require 2 injections in the same hand, but if more than 5 of 10 patients need 2 injections the costs would exceed those of fasciectomy. Our estimates of the costs assuming 20% would require 2 injections were based on separate treatment sessions; the costs would be even lower if the 2 injections are given in the same session, which would probably become the usual practice.[12] Further, our results should be considered conservative since we have not considered complications (such as wound infection and chronic regional pain syndrome) that are probably more frequent after surgery than after CCH injections and would therefore add to the total costs. The study by Hurst et al.[7] reported use of an average of about 2 CCH injections per patient. However, in that study finger extension, which often is a painful procedure, was done without anaesthesia, which may have reduced the degree of initial contracture correction and thus necessitating a second injection. As in our study, use of local anaesthesia is currently the standard procedure. In addition, Hurst et al. injected 0.58 mg CCH into one part of the cord whereas our technique is to inject the whole content of a single CCH injection (0.9 mg) into the cord at multiple sites, which would probably increase the efficacy of a single injection.

For fasciectomy, the largest cost was represented by the various costs associated with a day-surgery procedure of approximately 1 hour duration in the operating room. The cost would be lower if the average operating time were shorter than our estimate of 62 minutes. In a recent study of DC in 12 European countries (based on a surgeon survey and patient chart review),

the mean operating time for fasciectomy across all countries was 67 minutes (Nordic 63, Eastern 69, Western 66, and Mediterranean 68 minutes).[4] A potential advantage with CCH injections is the possibility to treat patients with bilateral disease in 1 stage, which is uncommon with surgery considering the nature of the procedure. In contrast, patients with contractures involving 3 or more fingers can be treated with surgery in one session, but would need at least 2 CCH injections and, in more severe cases, 2 or more treatment sessions.

Skin tears ranging from minor superficial skin breakage to deeper wounds occurred in more than half the patients after CCH injections in our study. Skin tears following CCH injections were reported in 11% in the multicenter randomized trial,[7] and in up to 19% in other studies.[13,14] Skin tears are more likely to occur in severe contractures especially of the small finger.[9] Because the incidence and severity of skin tears (ie, need for wound care) may vary we calculated the costs assuming that, on average, one third of the patients would require 1 nurse visit and also did a sensitivity analysis assuming an average of 1 nurse visit. We believe these estimates cover the costs of wound care even if the true incidence of skin tears is higher than previously reported.

We only compared direct costs, and therefore did not include costs of lost productivity or sick leave. Among employed patients, sick leave is more likely to be necessary and longer after fasciectomy than after CCH injections. According to the Swedish Social Insurance Agency the total cost of a 1-week sick leave based on the average salary in Sweden 2011 (including sick-pay, general payroll tax, vacation-pay and overhead costs) exceeds 1300 USD (www.scb.se). In addition, the direct costs of CCH injections and fasciectomy may differ across countries and settings. In a Canadian study that estimated the cost (during 2005) of open carpal tunnel release, a 10-minute procedure done under local anaesthesia, the total cost

(excluding surgeon's fee) was 137 CAD when done in the main operating room and 53 CAD dollars when done in the office.[15] Although the largest treatment cost for CCH injections was the cost of the injection itself, which may be substantially higher in some countries, the costs of surgery in these countries may also be higher. In a study involving 24 patients treated with fasciectomy at a single US hospital from 2008 to 2010 the average direct cost, defined as costs billed from hospital charges (facility fees) and professional charges (surgeon and anaesthesia fees) was estimated to be 11,240 USD.[9]

A limitation of our study is that only very short-term outcomes were measured. The improvement was high and the minor residual contracture was similar for CCH and fasciectomy. Differences in long-term outcomes may change the cost-effectiveness of these treatments because if they differ substantially in the recurrence rate and the need for further treatments the cost of subsequent treatments should also be considered. According to the most recent published data regarding recurrence after CCH injections (defined as contracture increase of 20 degrees or greater in the presence of a palpable cord in joints initially corrected to a maximum of 5-degree contracture), the overall rate in 623 joints at 3 years was 35% (MCP 27% and PIP 56%) but the recurrence required treatment in only 7%.[16] Following fasciectomy a 3-year recurrence rate of 12% has been reported in two studies; in the first study, 4 of 33 hands had more than 30 degrees increase in joint contracture compared to 6 weeks,[11]and in the second study, 11 of 90 fingers showed progressive recurrence of PIP joint contracture but no specific definition of recurrence was stated.[17] Thus, depending on the proportion of patients that subsequently need repeated treatment because of recurrent contracture in the treated fingers it is possible that in the long-term the direct costs of treatment with CCH may exceed those of fasciectomy.

Another limitation is that in the fasciectomy group the baseline range-of-motion measurements were done by different surgeons and the follow-up measurements by different therapists. The inter-observer reliability of these measurements is unknown and there might be a risk that the surgeon overestimated the preoperative contracture and the treating therapist underestimated residual contracture. However, we do not believe this issue has a substantial influence because fasciectomy was the only treatment option and the results of the post-treatment measurements, done by therapists, were similar in both groups.

In conclusion, treatment of DC with a single CCH injection costs 33% less, in direct costs, than fasciectomy with equivalent short-term efficacy (6 weeks) regarding reduction in contracture.

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**Table 1** Characteristics of the two samples of patients with Dupuytren's contracture treated with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | | CCH injection | Fasciectomy |
|---|---|---|---|
| Number of patients (men) | | 16 (11) | 16 (13) |
| Age (yrs), mean (SD) | | 69 (4) | 71 (5) |
| Number of fingers treated* | | | |
| Small | | 11 | 9 |
| Ring | | 7 | 8 |
| Middle | | 0 | 1 |
| Extension deficit (degrees) | | | |
| Total† | mean (SD) | 90 (39) | 71 (28) |
| | median (IQR) | 70 (60-115) | 75 (45-89) |
| MCP‡ | mean (SD) | 64 (16) | 60 (17) |
| | median (IQR) | 65 (60-75) | 60 (41-80) |
| PIP‡ | mean (SD) | 55 (22) | 46 (18) |
| | median (IQR) | 55 (43-70) | 40 (35-48) |

CCH, collagenase clostridium histolyticum; IQR, interquartile range

*2 patients in each group had 2 fingers treated.

† Metacarpophalangeal (MCP) plus proximal interphalangeal (PIP) joints in all treated fingers (in patients with 2 fingers treated the finger with largest extension deficit was used).

‡ The values showing MCP and PIP extension deficits separately include only joints with contracture (no MCP contracture in 1 patient in the CCH group and 2 patients in the fasciectomy group and no PIP contracture in 7 patients in each group).

**Table 2** Cost specification for the various stages of treating Dupuytren's contracture with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | **Personnel costs*** (USD) | **Other costs†** (USD) |
|---|---|---|
| Doctor visit, CCH or fasciectomy (doctor and nurse) | 65.80 | 16.78 |
| Injection, CCH (doctor and nurse) | 70.63 | 991.16 |
| Finger extension, CCH (doctor and nurse) | 70.63 | 20.97 |
| Therapist visit, CCH | 26.58 | 25.16 |
| Surgery, fasciectomy (doctors and others) | 783.97 | 380.81 |
| Day surgery care, fasciectomy | 88.10 | 52.41 |
| Therapist visit, fasciectomy | 39.88 | 37.77 |
| Nurse visit, CCH or fasciectomy | 43.51 | 37.77 |

CCH, collagenase clostridium histolyticum; USD, United States dollars

*Include average salary, social security contributions, vacation pay, sick pay, overhead costs, and the degree of capacity utilization.

†Include costs of surgical and other materials, injections, premises, etc.

Price of 1 CCH injection = 970.19 USD.

**Table 3** Number of visits to medical personnel, actual costs and short-term outcomes of treating Dupuytren's contracture with collagenase clostridium histolyticum injection or surgery (fasciectomy)

| | | CCH injection | Fasciectomy |
|---|---|---|---|
| Mean, median (IQR) number of visits to: | | | |
| Doctor | | 3* | 2* |
| Nurse | | 0.33* | 3.0, 3.0 (2.0-3.8) |
| Therapist | | 3* | 5.1, 4.0 (3.0-6.8) |
| Total cost per patient (USD) | | 1418.04 | 2102.56 |
| Total cost per patient when 20% require 2 injections (USD) | | 1675.24 | 2102.56 |
| Extension deficit (degrees)† | | | |
| Total | mean (SD) | 20 (25) | 19 (19) |
| | median (IQR) | 10 (0-30) | 10 (0-34) |
| MCP | mean (SD) | 10 (17) | 8 (10) |
| | median (IQR) | 0 (0-15) | 0 (0-20) |
| PIP | mean (SD) | 23 (18) | 21 (13) |
| | median (IQR) | 20 (8-35) | 25 (8-33) |

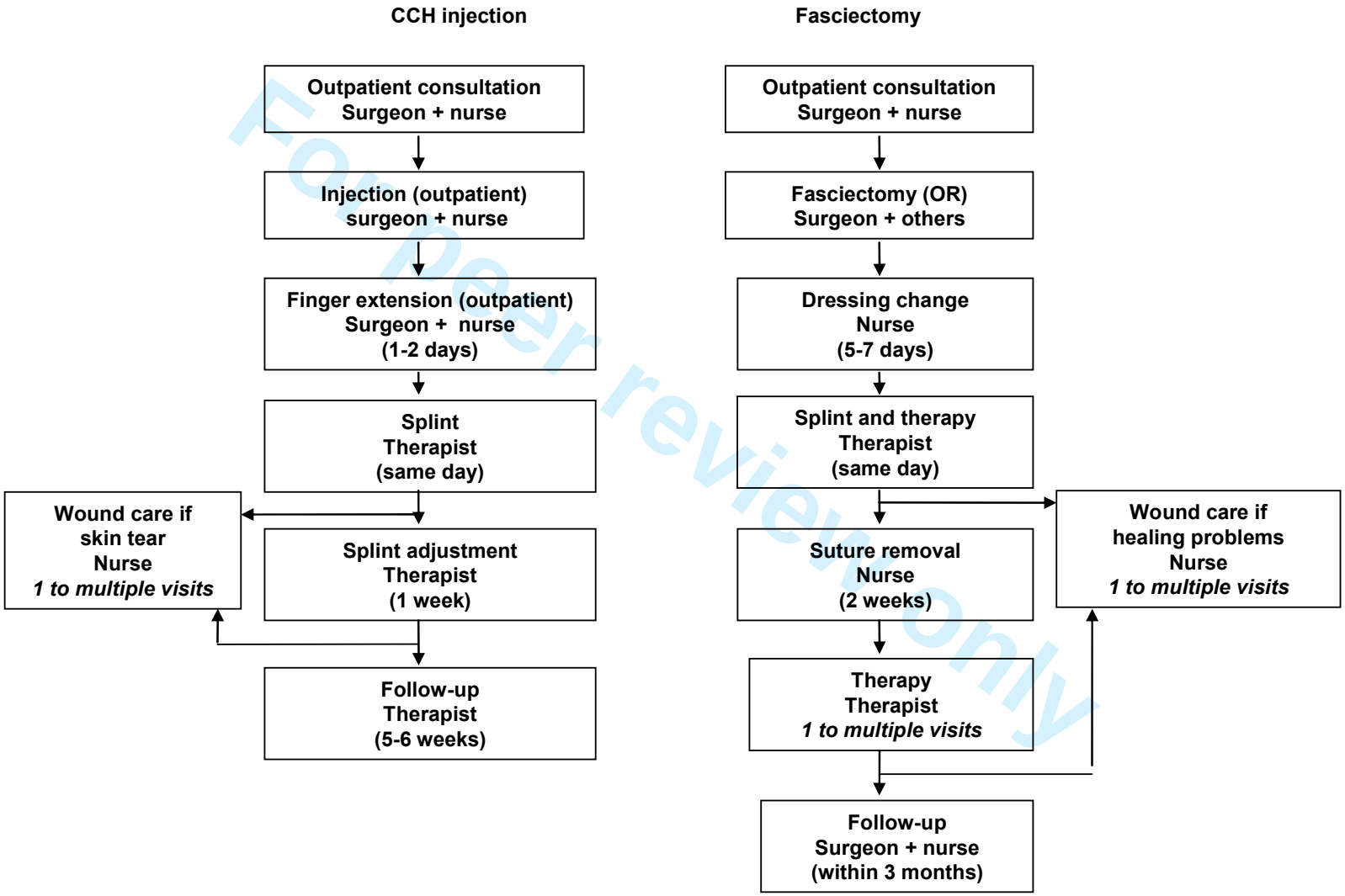
CCH, collagenase clostridium histolyticum; IQR, interquartile range; USD, United States dollars

* Number of visits to a doctor in both groups and to a therapist in the CCH group was similar for all patients (Figure 1); a third of CCH patients assumed to require 1 visit to a nurse.

† Metacarpophalangeal (MCP) plus proximal interphalangeal (PIP) joints in all treated fingers. The values showing MCP and PIP extension deficits separately include only joints with pretreatment contracture (see footnote in Table 1).

**Figure legend**

**Figure 1.** Diagram showing the various stages of treating patients with Dupuytren's contracture with collagenase clostridium histolyticum (CCH) injection or with fasciectomy as a day-surgery procedure performed in the operating room (OR). The number of visits is 1 unless specified otherwise.



STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** P 1+2 | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** | | |
| Background/rationale P 4-5 | 2 | Explain the scientific background and rationale for the investigation being reported |
| Objectives P 5 | 3 | State specific objectives, including any prespecified hypotheses |
| **Methods** | | |
| Study design P 6 | 4 | Present key elements of study design early in the paper |
| Setting P 6 | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants P 6 | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case |
| Variables P 8-10 | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/ measurement P 7-10 | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias P 10-11 | 9 | Describe any efforts to address potential sources of bias |
| Study size P 10 | 10 | Explain how the study size was arrived at |
| Quantitative variables P 10-11 | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods P 10-11 | 12 | (*a*) Describe all statistical methods, including those used to control for confounding |
| | | (*b*) Describe any methods used to examine subgroups and interactions |
| | | (*c*) Explain how missing data were addressed |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed<br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy |
| | | (*e*) Describe any sensitivity analyses |

Continued on next page

| | | |
|---|---|---|
| **Results** | | |
| Participants<br>**P 12**<br>**Figure 1** | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| | | (b) Give reasons for non-participation at each stage |
| | | (c) Consider use of a flow diagram |
| Descriptive data<br>**P 12, Table 1** | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) |
| Outcome data<br>**P 12-13**<br>**Table 2 & 3** | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures |
| Main results<br>**P 12-13**<br>**Table 2 & 3** | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (*b*) Report category boundaries when continuous variables were categorized |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Other analyses<br>**P 12-13** | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | | |
| Key results<br>**P 14** | 18 | Summarise key results with reference to study objectives |
| Limitations<br>**P 15-16** | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Interpretation<br>**P 15-16** | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalisability<br>**P 15** | 21 | Discuss the generalisability (external validity) of the study results |
| **Other information** | | |
| Funding<br>**P 17** | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.