Contact allergy (CA) is prevalent in patients with chronic leg ulcers (CLUs) due to venous stasis and may delay wound healing. Exposure to different ointments and wound dressings over time, combined with occlusive bandaging, may predispose to contact sensitization. The spectrum of allergens depends on wound care practices. Studies on CA in patients with CLUs from Norway are lacking. To determine the occurrence of CA in patients with CLUs, patch testing was performed with the Leg Ulcer Series (LUS) containing 27 chemicals and five additional substances relevant to wound treatment: Caine mix III and V, hydrocortisone, IntraSite gel (propylene glycol 20%, Smith & Nephew), and Brulidine (dibrompropamidine 0.15%, Sanofi-Aventis) (Table S1). Fifty-two of the 97 patients were also tested with the European Baseline Series (EBS) (Table S2).

RESULTS AND DISCUSSION
A total of 97 patients were tested (61 women, 36 men; median age 78 years, range 34–99 years). Mean duration of ulcer was 3.8 years (range 6 weeks–40 years). For the LUS patch test with five additional substances, a positive patch test was detected in 31 of the 97 patients (32%). The most frequent allergens were wood tar mix, benzalkonium chloride, fusidic acid, IntraSite gel, budesonide, and hydrocortisone-17-butyrate (Figure 1A). All these are relevant to wound treatment as they are constituents of standard wound dressing procedures in Norway. The findings are also in line with studies from other countries. Benzalkonium chloride and fusidic acid are not recommended in chronic wound care but are widely used in primary care as constituents of OTC preparations. Benzalkonium chloride is often used in wet wipes, and our results suggest that antiseptic wipes should not be used in these patients. Five of the patients had an allergic reaction to IntraSite gel, but none of these had a positive reaction to the ingredient propylene glycol when tested alone. This could be explained by a reaction to some other constituent of IntraSite gel, for instance carbamoylmethyl cellulose, which has been previously reported, or by a difference in concentration of the test substances. IntraSite gel contains 20% propylene glycol, while the concentration of the test substance in LUS is only 5% (Table S1). Topical steroids are highly relevant because of the high prevalence of leg eczema in this patient group. CA to budesonide and hydrocortisone-17-butyrate could indicate allergy against any topical.
steroid because of cross-reactions; use tests are needed to clarify. We chose to include Brulidine because it is widely used as an OTC preparation in Norway and CA has been previously described. Only two patients in our study had a positive reaction to Brulidine (+ and ++, respectively).

For the EBS patch test, 27 of the 52 patients tested (52%) had positive reactions and Myroxylon pereirae, fragrance mix, and colophonium were the most frequent allergens (Figure 1B), consistent with previous findings. A reaction to wood tar mix could also indicate cross-sensitivity to colophonium.

Forty per cent of the patients with a positive patch test had one reaction, 33% of the patients had two reactions, 10% had three reactions while 17% had four or more reactions simultaneously. When tested with both series, some substances were tested twice, for instance Budesonide that occurs in both tests in the same concentration. Patients with a strong reaction tended to have consistent reactions, but weak reactions were not consistent.

This could be explained by some weak reactions being, in fact, false-positives.

Taking only one reading is clearly a limitation to our study, and test readings on D5 and D7 would have been ideal so as not to miss any late reactions. A single reading on D3 was a practical compromise as our patient population was elderly, relatively immobile, and had to travel long distances.

Our findings confirm a high prevalence of CA in patients with venous CLUs. These patients should be patch tested routinely with both LUS and EBS to exclude topical treatment that may delay wound healing.

**AUTHOR CONTRIBUTIONS**

Astrid Lossius: Data curation; formal analysis; investigation; methodology; writing-original draft. Merete Lorentzen: Conceptualization; data curation; investigation; methodology; writing-review and editing. Joar Austad: Conceptualization; data curation; formal analysis; methodology; project administration; supervision; writing-review and editing. Tone Bergersen: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; writing-review and editing.
REFERENCES


SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.