

## Scabies Management Outcomes: Identification of Risk Factors for Treatment Success or Failure

Vanessa Azzolina<sup>1\*</sup>, Franziska Schauer<sup>1\*</sup>, Julia Felicitas Pilz<sup>2</sup>, Alexander Zink<sup>2,3</sup>,  
Kilian Eyerich<sup>1,3</sup>, Anna Caroline Pilz<sup>1</sup>

\* These authors have contributed equally

1 Department of Dermatology and Venereology, Medical Center, University of Freiburg, Freiburg, Germany

2 Department of Dermatology and Allergy, Technical University of Munich, School of Medicine and Health, Munich, Germany

3 Division of Dermatology and Venereology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden

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**Corresponding Author:** Anna Caroline Pilz, Department of Dermatology and Venereology, Medical Center, University of Freiburg, Hauptstraße 7, 79104 Freiburg, Germany. ORCID: 0000-0002-3028-4556. E-mail: [anna.caroline.pilz@uniklinik-freiburg.de](mailto:anna.caroline.pilz@uniklinik-freiburg.de)

**ABSTRACT Introduction:** Scabies is a parasitic infectious skin disease classified as a neglected tropical disease by the World Health Organization in 2017. Currently, it is becoming a major challenge in high-income countries, with rapidly rising incidence and increasing reports about treatment failure.

**Objectives:** Factors that are associated with treatment failure or success were evaluated.

**Methods:** This non-interventional prospective observational study was conducted as a questionnaire survey at the Department of Dermatology and Venereology of the University of Freiburg from January to November 2023. Patients that still suffered from scabies 2–6 weeks after medical treatment were classified as “failure”; those who were free of scabies belonged to the success group.

**Results:** Of 102 participants, with a mean age of  $34.4 \pm 17.3$  years (male: 60.4%), 77 (75.5%) were assigned to the success and 25 (24.5%) to the failure group. A larger proportion of the latter was clinically more severely affected, applied permethrin monotherapy, did not undertake special decontamination measures, but used alcohol as a disinfectant. Treatment success was associated with an additional systemic treatment, a repeated intake of ivermectin, and intensified decontamination measures such as storage of clothes in plastic bags for four days or vacuum cleaning of car seats.

**Conclusions:** Our findings indicate that a consistent second-dose administration of ivermectin and refraining from permethrin monotherapy may be advisable.

## Introduction

Scabies is a parasitic skin disease caused by the mite *Sarcoptes scabiei varietas hominis*, leading to an intensely itching rash [1]. It is mainly spread by direct skin-to-skin contact and therefore also considered a sexually transmitted disease [2,3]. Typical lesions are small tunnels, burrowed by the female mites, and eczematous lesions such as vesicles, papules, and excoriations as well as possible signs of impetiginization [4]. Predominantly affected body areas are those that are relatively warm and have a thin corneal layer like the interdigital spaces, wrists, axillae, and the genital area [5]. Approximately 175 million people are infested with scabies worldwide [6]. The highest prevalence is found in developing tropical countries such as those in the Pacific Islands region [7], leading to the classification of scabies as a neglected tropical disease by the World Health Organization (WHO) in 2017 [8]. Scabies is also becoming problematic in high-income countries like the United States and Norway [9,10]. In Germany, for example, analyses of statutory health insurance funds showed a nine-fold increase in scabies diagnoses from 2009 to 2018. The highest incidence was seen in 15-to-19-year-olds. Moreover, in the same time period, a 14-fold increase in prescriptions for scabicides and an increased percentage of repeated applications of treatments were observed [11]. The latter serves as an indicator of an increased number of cases of treatment failure. Various reasons have been attributed to treatment failure, including increased drug resistances of mites, lack of compliance, and insufficient treatment of contact persons [11–14]. Furthermore, scabies treatment itself is time-consuming and complex, consisting of topical and/or systemic drugs as well as treatment of contact persons and hygiene measures to decontaminate surroundings [15]. Individual aspects, such as severity of disease, environmental settings of the patients, sources of information, modes of therapy applications, and hygiene measures implemented may differ between patients and can therefore also affect treatment response.

## Objectives

The aim of this study was to identify factors influencing treatment failure and success by comparing scabies patients who were treated successfully with patients who still suffered from scabies after treatment.

## Methods

### Survey and Patients

This non-interventional prospective cross-sectional study was conducted as a pseudonymized and voluntary paper-based questionnaire at the Department of Dermatology and

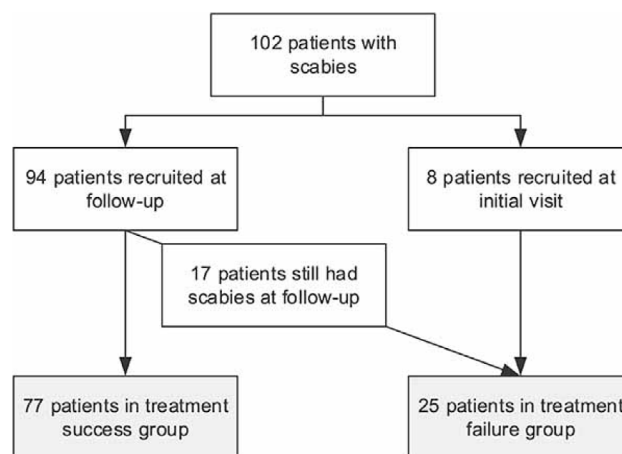


Figure 1. Patient flowchart

Venereology, Medical Center, University of Freiburg, between January 2023 and November 2023. The diagnosis of scabies was made if a mite and/or feces and/or eggs were identified via dermoscopy and/or microscopic analysis of skin scrapings. Cure of scabies was defined by absence of fresh lesions combined with absence of mites and/or feces and/or eggs in remaining healing lesions. Participants had to be 18 years or older, had to provide written informed consent before participating, and had been diagnosed with classical scabies in our outpatient clinic. Patients were recruited two to six weeks after completion of scabies treatment and were assigned to one of two groups based on their treatment outcome (Figure 1). The “success group” included patients who were free of scabies at their follow-up appointment, which took place 3–6 weeks after their initial visit at out clinic. For the “failure group,” two different routes of recruitment were applied: a) patients were included at follow-up if they still had scabies at that time, or b) patients were already recruited at the initial visit if they had undergone externally prescribed scabies treatment within the six weeks prior to the visit and suffered from persisting scabies. The study was reviewed and approved by the Ethics Committee of the Faculty of Medicine of the University of Freiburg (23-1019-S1).

### Questionnaire

The questionnaire was developed by a multidisciplinary team of dermatologists and an epidemiologist and contained a short physician-based introductory part (five questions) and a main part (34 questions) to be completed by the patients. Physicians provided details concerning the diagnosis and disease severity. The main part was divided into three sections: (1) a) patient and b) disease characteristics, (2) details of last medical treatment, and (3) decontamination measures of surroundings. Section 1: a) age, sex, height, weight, native language, highest education qualification, number of household members, number of children in household, age

of children; b) suspected location of transmission, sources of information. Section 2: the last topical and systemic therapies applied and their mode of application, treatment status of household members. Section 3: hygiene measures for clothing, bed linens, mattresses, carpets, and car seats; disinfectants used.

## Statistical Analyses

Descriptive data were generated using mean and standard deviation (SD) as well as absolute numbers and proportions. Unpaired t-tests were used for metric variables and Levene's test was used to assess the homogeneity of variance. Pearson's chi-squared test and Fisher's exact test were performed for nominally scaled variables. Alpha was set at 0.05. All paper-based questionnaires were digitalized using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at the Center for Digitization and Information Technology at the University Medical Center Freiburg [16,17]. Data analysis was performed using IBM SPSS Statistics (Version 29, IBM Corporation, Armonk, NY, USA).

## Results

### Patient and Disease Characteristics

A total of 102 scabies patients (male: 60.4%) with a mean age of  $34.4 \pm 17.3$  years were recruited during their medical consultations at our outpatient clinic. Of these, 77 (75.5%; treatment success group) were free of scabies and 25 (24.5%; treatment failure group) had persisting scabies. Seventeen (68%) of the latter group had been initially treated at our outpatient clinic, and eight (32%) treated externally. Regarding sex (success: 59.2% vs. failure: 64.0%;  $P=0.671$ ), age (success:  $35.8 \pm 18.3$  vs. failure:  $29.8 \pm 12.9$ ;  $P=0.077$ ), and body mass index (BMI; success:  $24.8 \pm 4.9$  vs. failure:  $25.9 \pm 6.7$ ;  $P=0.430$ ), no difference between the groups was observed. The number of household members (success:  $2.1 \pm 1.2$  vs. failure:  $1.8 \pm 1.1$ ;  $P=0.313$ ) and children (success:  $0.7 \pm 1.1$  vs. failure:  $0.8 \pm 1.0$ ;  $P=0.575$ ) as well as the children's mean age did not differ (success:  $12.0 \pm 7.7$  vs. failure:  $10.2 \pm 7.0$ ;  $P=0.487$ ; Table 1). Analyzing disease severity, all patients in the failure group ( $N=25$ , 100%) were classified with a physician global assessment (PGA)  $\geq 2$ , but only 84% of the success group ( $N=65$ ) had such a high PGA. However, the number of affected body parts amounted equally to  $5.3 \pm 3.0$  in both groups (Table 1). Regarding the location of transmission, a larger proportion of the success group suspected private contacts (success: 50.6% vs. failure: 28.05%;  $P=0.048$ ). 81.4% ( $N=83$ ) of all participants received oral and/or written information about scabies from their physicians (success: 80.5% vs. failure: 84.0%;  $P=1.000$ ), with no difference between the groups in terms of the individual

sources of information used or their total number (success:  $2.1 \pm 1.3$  vs. failure:  $1.9 \pm 1.2$ ;  $P=0.488$ , Table 1).

### Last Drug Treatment

Concerning medical drugs used for the last treatment, 97.1% underwent topical treatment with permethrin (Table 2), while only a fraction of people used other topical treatments such as benzyl benzoate and/or a combination of different cremes. About three-quarters (75.5%,  $N=77$ ) applied permethrin twice, with no difference between the groups. However, two trends concerning permethrin application were observed. Firstly, 61.0% of the success group left the cream on the body  $\geq 12$  hours opposed to 40.0% of the failure group ( $P=0.066$ ), and 82.9% of the success group sought help from a second person for the application of topical treatments (failure: 66.7%;  $P=0.089$ ). An additional systemic treatment was taken by 93.5% in the success group and 76.0% in the failure group ( $P=0.024$ ). This means only 5.2% ( $N=4$ ) of the successful participants received permethrin monotherapy, as opposed to 24.0% ( $N=6$ ;  $P=0.013$ ) in the failure group. Furthermore, a larger proportion of patients in the success group received ivermectin twice (success: 81.7% vs. failure: 50.0%;  $P=0.010$ ). The proportions of participants with whole household treatment did not differ between the success and the failure group (data not shown).

### Decontamination Measures of Surroundings

In the success group, 37% changed their bed linens daily for  $\geq 4$  days after application of the topical therapy compared to 16% in the failure group ( $P=0.044$ ; Table 3). In addition, the proportion of patients that stored clothes such as pants and pullovers in plastic bags at room temperature for four days was larger in the success than in the failure group (success: 62.3% vs. failure: 28.0%;  $P=0.003$ ). A larger proportion of participants in the failure group did not undertake particular hygiene measures regarding objects such as carpets (success: 22.1% vs. failure: 52.0%;  $P=0.004$ ) or car seats (success: 33.8% vs. failure: 68.0%;  $P=0.003$ ). Instead, patients in the success group vacuum-cleaned their car seats in 48.1% of the cases (vs. failure: 20.0%;  $P=0.013$ ). Overall, disinfection of mattresses, carpets, and car seats was conducted by about one-third (27.8%) of the participants, but no difference in the proportion of patients disinfecting particular items was observed. Nevertheless, more patients in the failure group used alcohol as a disinfectant (success: 18.2% vs. failure: 40.0%;  $P=0.025$ ).

## Discussion

The aim of the present study was to assess different factors between patients with a successful or failed treatment for scabies. Participants of the treatment failure group were

**Table 1. Patient and Disease Characteristics of the Two Studied Treatment Groups.**

	Treatment Status		P-value
	Success (N=77)	Failure (N=25)	
Demographics			
Male sex, N (%), N <sub>s</sub> =76, N <sub>f</sub> =25	45 (59.2)	16 (64.0)	0.671 <sup>a</sup>
Age in years, mean ± SD	35.8 ± 18.3	29.8 ± 12.9	0.077 <sup>c</sup>
Body mass index, mean ± SD, N <sub>s</sub> =76, N <sub>f</sub> =23	24.8 ± 4.9	25.9 ± 6.7	0.430 <sup>c</sup>
Household			
Number of total members, mean ± SD	2.1 ± 1.2	1.8 ± 1.1	0.313 <sup>c</sup>
Number of children, mean ± SD	0.7 ± 1.1	0.8 ± 1.0	0.575 <sup>c</sup>
Age of children, mean ± SD, N <sub>s</sub> =28, N <sub>f</sub> =12	12.0 ± 7.7	10.2 ± 7.0	0.487 <sup>c</sup>
Disease severity			
Physician global assessment ≥ 2	65 (84.4)	25 (100.0)	0.035 <sup>b</sup>
Number of affected body parts, mean ± SD	5.3 ± 3.0	5.3 ± 3.0	0.945 <sup>c</sup>
Suspected location of transmission			
Workplace, N (%)	3 (3.9)	3 (12.0)	0.156 <sup>b</sup>
Workplace (professional nursing), N (%)	5 (6.5)	1 (4.0)	1.000 <sup>b</sup>
Hospital/nursing home (as visitor), N (%)	0 (0.0)	0 (0.0)	-
Sport/recreation-center, N (%)	3 (3.9)	0 (0.0)	1.000 <sup>b</sup>
Private contact, N (%)	39 (50.6)	7 (28.0)	0.048 <sup>a</sup>
Hotel, N (%)	12 (15.6)	4 (16.0)	0.960 <sup>a</sup>
Public transport, N (%)	2 (2.6)	0 (0.0)	1.000 <sup>b</sup>
Unknown/Other, N (%)	31 (40.3)	13 (52.0)	0.303 <sup>a</sup>
Sources of information			
Oral and/or written information by physician, N (%)	62 (80.5)	21 (84.0)	1.000 <sup>b</sup>
Package inserts of drugs, N (%)	27 (27.3)	6 (24.0)	0.747 <sup>a</sup>
Pharmacy, N (%)	14 (18.2)	4 (16.0)	1.000 <sup>b</sup>
Friends, N (%)	18 (23.4)	3 (12.0)	0.222 <sup>a</sup>
Internet, N (%)	45 (58.4)	13 (52.0)	0.572 <sup>a</sup>
Other, N (%)	1 (1.3)	0 (0.0)	1.000 <sup>b</sup>
No information, N (%)	7 (9.1)	2 (8.0)	1.000 <sup>b</sup>
Number of sources of information, mean ± SD	2.1 ± 1.3	1.9 ± 1.2	0.488 <sup>c</sup>

<sup>a</sup>Pearson's chi-squared test. <sup>b</sup>Fisher's exact test for nominally scaled variables. <sup>c</sup>Unpaired t-test for metrically scaled variables. *Abbreviations:* f = failure; N = number; SD = standard deviation; s = success.

clinically more severely affected, more often applied permethrin monotherapy, and undertook special decontamination measures less frequently but used alcohol as disinfectant more often. Treatment success was linked to an additional systemic treatment with a repeated dosage of ivermectin and certain intensified hygiene measures, such as a daily change of bed linens for ≥4 days after application of ointment, or vacuum-cleaning of car seats. Overall, the analyzed groups were similar regarding distribution of sex and age; members of the failure group tended to be younger. Analyses of claims data from 2009-2018 of outpatients insured by German statutory health insurance companies showed that the 15-to-19-year-old age group presented the highest incidence of scabies as well as the highest percentage of repeated prescriptions

of scabies treatment [11]. In the study described here, only adults were included, but the trend of somewhat younger patients being more prone to treatment failure was confirmed. No difference concerning household size, number of children, and/or age of children was seen in our study. Aussy et al., who investigated risk factors for treatment failure of scabies in France, did not observe any difference concerning household size, presence of children, or type of childcare either [18]. This implies that although scabies is more prevalent in larger households [19], treatment failure is not a particular issue there. All patients in the failure group had a PGA ≥2 as opposed to 84% of the success group, indicating a more severe disease and thus indirectly a longer disease duration. We did not assess the total number of scabies treatments,

**Table 2. Last Drug Treatment of the Two Studied Treatment Groups.**

	Treatment Status		P-Value
	Success (N=77)	Failure (N=25)	
Applied topical treatment			
Permethrin, N (%)	75 (97.4)	24 (96.0)	1.000 <sup>b</sup>
Benzyl benzoate, N (%)	4 (5.2)	2 (8.0)	0.633 <sup>b</sup>
Crotamiton, N (%)	0 (0.0)	0 (0.0)	-
Other, N (%)	3 (3.9)	0 (0.0)	1.000 <sup>b</sup>
Number of permethrin applications			0.506 <sup>b</sup>
1x, N (%)	10 (13.0)	4 (16.0)	
2x, N (%)	60 (77.9)	17 (68.0)	
Other, N (%)	7 (9.1)	4 (16)	
Duration of application ≥ 12h	47 (61.0)	10 (40.0)	0.066 <sup>a</sup>
Help of 2nd person with application, Ns=76, Nf=24	63 (82.9)	16 (66.7)	0.089 <sup>a</sup>
Additional systemic treatment	72 (93.5)	19 (76.0)	0.024 <sup>b</sup>
Permethrin monotherapy	4 (5.2)	6 (24.0)	0.013 <sup>b</sup>
Number of doses of ivermectin, Ns=71, Nf=18			0.010 <sup>b</sup>
1x, N (%)	8 (11.3)	7 (38.9)	
2x, N (%)	58 (81.7)	9 (50.0)	
Other, N (%)	5 (7.0)	2 (11.1)	

<sup>a</sup>Pearson's chi-squared test. <sup>b</sup>Fisher's exact test for nominally scaled variables. *Abbreviations:* f = failure; N = number; s = success.

**Table 3. Decontamination Measures of Surroundings of the Two Studied Treatment Groups.**

	Treatment status		p-Value
	Success (N=77)	Failure (N=25)	
<b>Daily change of bed linens for ≥4 days after application of cream</b>	29 (37.7)	4 (16.0)	0.044 <sup>a</sup>
<b>Clothes stored in plastic bag at RT for 4 days</b>	48 (62.3)	7 (28.0)	0.003 <sup>a</sup>
<b>Mattresses</b>			
Vacuum-cleaned, N (%)	56 (72.7)	14 (56.0)	0.117 <sup>a</sup>
Disinfected, N (%)	21 (27.3)	9 (36.0)	0.405 <sup>a</sup>
Other (e.g., drycleaning), N (%)	23 (29.9)	3 (12.0)	0.075 <sup>a</sup>
No particular measure, N (%)	5 (6.5)	4 (16.0)	0.217 <sup>b</sup>
<b>Carpets</b>			
Vacuum-cleaned, N (%)	48 (62.3)	11 (44.0)	0.107 <sup>a</sup>
Disinfected, N (%)	15 (19.5)	2 (8.0)	0.230 <sup>b</sup>
Other (e.g., drycleaning), N (%)	13 (16.9)	1 (4.0)	0.179 <sup>b</sup>
No particular measure, N (%)	17 (22.1)	13 (52.0)	0.004 <sup>a</sup>
<b>Car seats</b>			
Vacuum-cleaned, N (%)	37 (48.1)	5 (20.0)	0.013 <sup>a</sup>
Disinfected, N (%)	14 (18.2)	3 (12.0)	0.554 <sup>b</sup>
Other (e.g., drycleaning), N (%)	8 (10.4)	1 (4.0)	0.447 <sup>b</sup>
No particular measure, N (%)	26 (33.8)	17 (68.0)	0.003 <sup>a</sup>
<b>Disinfectants</b>			
Alcohol (ethanol/ propanol), N (%)	14 (18.2)	10 (40.0)	0.025 <sup>a</sup>
Permethrin/ esbiothrin/ pyrethrum, N (%)	2 (2.6)	0 (0.0)	1.000 <sup>b</sup>
Other, N (%)	21 (27.3)	3 (12.0)	0.118 <sup>a</sup>

<sup>a</sup>Pearson's chi-squared test, and <sup>b</sup>Fisher's exact test for nominally scaled variables. *Abbreviations:* f = failure; N = number; RT = room temperature; s = success.



but with prolonged disease duration, treatment may become more difficult due to enhanced secondary dermatitis, sensitization to topical scabicides, or drug resistance [20]. In addition, a larger proportion of the success group suspected private contacts as the location of transmission. Since classical scabies is almost exclusively transmitted via skin-to-skin contact, it is in general more likely that private contacts and/or professional nursing activities are sources of transmission [21]. Thus, the observed difference here might indicate that patients in the success group knew more about scabies and were more attentive towards the treatment. Surprisingly, only 81.4% of all patients reported having received information about the disease from physicians. There was no difference between the groups regarding the number of sources of information or the format used. Since scabies treatment is relatively complex, access to written information from a physician can contribute to treatment success [18]. 97.1% of the participants used permethrin creme, the recommended first-line therapy in Germany [15]. There was no difference between one or two applications with regard to treatment success. The same observation was made by Aussy et al. [18]. However, in the French study, topical benzyl benzoate was used instead of permethrin. Permethrin is known to be acaricidal and ovicidal [15], and a single application should therefore be sufficient, if applied correctly. Concerning duration of application of permethrin, 8–12 hours or overnight is usually advised in Germany [15]. The results presented here suggest that it may be an advantage to prolong the duration of application to 12 hours or more. Furthermore, a trend for an association between help from a second person and therapeutic success was observed in this study. This is in line with German guidelines, in which assistance from a second person for topical treatment application is mentioned [15]. Our data show a beneficial effect of the additional systemic treatment. In France, the combination of benzyl benzoate and ivermectin was also more effective than a monotherapy with one of the substances [18]. At the same time, we observed that permethrin monotherapy is linked to treatment failure. Blaizot et al. also showed this association in French Guiana [22], and a recent randomized controlled trial in Austria found a heavily reduced cure rate of 27% for permethrin compared to 87% for benzyl benzoate [23]. Furthermore, a knockdown mutation leading to permethrin resistance was identified in *Sarcoptes scabiei varietas hominis* in 2023 [24]. Thus, a combination of two treatment strategies with different routes of administration and modes of action seems reasonable. Concerning the number of ivermectin doses, our study nicely demonstrates an association between repeated dose and success. As ivermectin is not

ovicidal, a second dose administration appears logical [25]. This is in line with the results of a study by Balestri et al. and also a recent meta-analysis [26,27]. Ivermectin monotherapy was not administered in our study but should in general be viewed critically since the development of resistances has been extensively described [28–30]. With regard to decontamination, washing laundry at temperatures above 50°C and storage of clothes in sealed plastic bags for at least three days at room temperature are recommended in the current German national guideline [15]. Changing bed linens daily for 3–4 days after application of topicals is proposed in package inserts of permethrin [31]. We found that treatment success was indeed linked to storage of clothes in plastic bags at room temperature and changing bed linens daily for at least four days after application. Additionally, more members in the success group vacuum-cleaned their car seats, and patients in the failure group applied particular decontamination measures less frequently. It is possible that patients in the failure group followed treatment guidelines less carefully in general. Consequently, the single decontamination measure itself might not be of the utmost importance, but a general willingness to follow the recommendations would be needed. Notably, more members in the failure group used alcohol-based disinfection. Cinotti et al. demonstrated that topical antiseptics did not reduce mite viability [32]; since alcohol is in general an effective disinfectant, people might easily have a false sense of security. In the French study, decontamination of furnishings was associated with treatment success, but here acaricides containing neopynamin and sumithrin were used [18].

## Limitations

Since this study has an observational and not an experimental design, all results are at most associations and have to be interpreted with caution. Confounders may be present and/or unevenly distributed. As in all questionnaire studies, there may have been recall bias. The exact procedure can be difficult to remember, especially if multiple treatments for scabies were administered. The study population, and especially the failure group, was relatively small. Additionally, selection bias may be present. Some members in the failure group reported on their externally prescribed treatments, and patients treated at a university hospital in general could have more severe disease symptoms and failed prior therapies. No information about the total number of treatments or the time between onset of symptoms and first treatment was collected. Moreover, the questionnaire consisted of non-standardized questions, but this is explained by the explorative approach of the study.

## Conclusions

In summary, our findings indicate that a consistent second dose of ivermectin and refrainment from permethrin monotherapy may be advisable.

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