

# Clinical characteristics and comorbidities of the most common atypical wounds in Northern Finland in 1996–2019: A retrospective registry study

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## Abstract

**Background and Aims:** Atypical wounds comprise about 20% of all chronic wounds. Their diagnosis and treatment are challenging and require multidisciplinary cooperation. More knowledge is needed about the clinical characteristics and comorbidities of atypical wounds to enhance the treatment of these wounds.

**Methods:** We studied clinical characteristics and comorbidities of the atypical wounds by using the patient data retrieved from the Oulu University Hospital patient database from the year 1996 to the end of 2019 with the following International Classification of Diseases codes: L88, L95.0, L95.8, L95.9, and L98.1.

**Results:** In our data, there were 135 patients with atypical wound, more commonly seen in females ( $N = 84$ , 62.2%) than in males ( $N = 51$ , 37.8%) ( $p < 0.05$ ). The mean age of patients at the time of diagnosis was 57.3 years; those with pyoderma gangrenosum (PG) and factitious wounds were the youngest (53.1 and 53.0 years, respectively). The majority of subjects ( $N = 126$ , 93.3%) were diagnosed with comorbidity at the time of the diagnosis. The most common type of wound was PG ( $N = 49/135$ , 36.3%), followed by vasculitis and factitious wounds. The prevalence of inflammatory bowel diseases and rheumatoid arthritis in PG patients was high (18.4% for both). All patients with Martorell hypertensive ischemic leg ulceration/calciophylaxis had a diagnosis of hypertension and diabetes mellitus. Psychiatric diseases were more common in patients with factitious wounds than in other types of wounds, whereas patients with vasculitis wounds had more commonly hypertension, obesity, and diabetes mellitus; however, these did not reach statistical significance.

**Conclusion:** Specific comorbidities associated with atypical wounds, such as high psychiatric comorbidity in factitious wounds. There is a female predominance in

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atypical wounds and patients are typically younger than patients with other types of wounds. Recognition of the typical clinical picture and comorbidities of atypical wounds may help in identifying these patients and thus also improving their treatment.

#### KEYWORDS

atypical wound, comorbid, factitious wound, Martorell HYTILU, pyoderma gangrenosum, vasculitis

## 1 | INTRODUCTION

The number of chronic wounds is estimated to increase with the aging of the population.<sup>1,2</sup> The most common chronic wounds are venous, arterial, or mixed wounds and pressure or diabetic foot ulcer.<sup>3</sup> Wounds that do not fit into these categories are called atypical wounds, comprising approximately 20% of chronic wounds.<sup>3,4</sup> The most common types of atypical wounds are pyoderma gangrenosum (PG), Martorell hypertensive ischemic leg ulceration (Martorell HYTILU), calciphylaxis, vasculitis, and factitious ulcers.<sup>4</sup> The factors behind atypical wounds are multifactorial, including inflammation or chronic illnesses.<sup>5</sup>

PG is an inflammatory neutrophilic dermatosis<sup>6</sup> with an annual prevalence estimated at 0.57–0.71/100,000 in Europe.<sup>7</sup> Its pathophysiology consists of a complex systemic autoinflammatory response, which is not fully understood.<sup>3,6</sup> Clinically it appears as papules or pustules, which progress into painful, deep ulcers in a few days.<sup>3</sup>

Martorell HYTILU and calciphylaxis share a similar clinical appearance of ischemic arteriosclerosis and acral necrosis.<sup>3</sup> In Europe, Martorell HYTILU represents 10%–15% of the leg ulcer patients hospitalized in the dermatological ward,<sup>7</sup> but the disease may be underdiagnosed due to lack of exact diagnostic criteria.<sup>8</sup> Martorell HYTILU is associated with long-term essential hypertension and Type 2 diabetes.<sup>3,8</sup> In turn, calciphylaxis is most typically associated with end-stage renal disease (ESRD), but in rare cases it is also seen in patients without ESRD and in connection with warfarin usage.<sup>3,9,10</sup> In patients undergoing dialysis, the prevalence of calciphylaxis varies between 0.04% and 4%.<sup>9</sup>

Vasculitis can be a primary process or a phenomenon secondary to medication, infection, or the presence of a systemic disease or a local factor such as trauma.<sup>9–11</sup> Its pathomechanisms include immunological reaction and inflammation of the blood vessels, which leads to vascular damage and even to skin ulceration.<sup>10</sup> Vasculitis wounds account for about 5%–13% of all chronic wounds.<sup>2,12–14</sup>

Contrary to other atypical wounds, a factitious ulcer is a self-inflicted skin lesion<sup>15</sup> diagnosed by exclusion. It is primarily associated with psychiatric disorders, most commonly personality disorders.<sup>16,17</sup> Specific diagnostic criteria have been proposed for these wounds, including young age and obvious location of the wound.<sup>18</sup>

Even though up to one in every five chronic wounds is classified as atypical, the epidemiological studies addressing these are scarce. We aimed to study the characteristics and comorbidities of the patients whose atypical wounds (including PG, vasculitis, factitious wounds, and Martorell HYTILU/calciphylaxis) have been treated in the Department of Dermatology in the Oulu University Hospital (OUH).

## 2 | MATERIALS AND METHODS

Patient data were retrieved from the OUH patient database from the year 1996 to the end of 2019 by using the following International Classification of Diseases (ICD) codes: PG L88, calcinosis cutis L94.2, vasculitis livedoides L95.0, skin limited vasculitis L95.8 and L95.9, and factitious dermatitis L98.1. All the patients with a selected diagnosis code for atypical wound as well as clinically described ulceration were included in the study, and data about preselected comorbidities at the time of the diagnosis (Table 1) were gathered from their medical records by the authors. Malignant ulcers, infectious ulcerations, and inflammatory wounds were not included since they are more rarely seen in clinical practice. The Medical Director of the OUH had approved the study.

### 2.1 | Ethical statement

No permission from an ethics committee or informed consent was required since the study was retrospectively based on medical report records.

### 2.2 | Statistical analyses

The overall prevalence of atypical wounds was calculated. Mean and standard deviation (SD) for age were calculated, and the categorical variables were presented as proportions. Mean differences between diagnosis groups for age at diagnoses were tested by independent samples *t*-test and analysis of variance and by Pearson's  $\chi^2$  test for categorical variables or Fisher's exact test, as appropriate. Statistical analyses were conducted using the R software package version 4.0.2 (<https://cran.rstudio.com>).

**TABLE 1** Characteristics of the study population ( $n = 135$ )

	Pyoderma gangrenosum (N = 49)	Martorell HYTILU/calciphylaxis (N = 6)	Factitious ulcer (N = 38)	Vasculitic ulcer (N = 42)	Total (N = 135)	p Value
Age						0.002
Mean (SD)	53.1 (18.2)	63.2 (15.4)	53.0 (18.0)	65.2 (17.2)	57.3 (18.4)	
Range (years)	16.0–91.0	43.0–79.0	8.0–85.0	17.0–92.0	8.0–92.0	
Sex, N (%)						0.027
Female	36 (73.5)	2 (33.3)	26 (68.4)	20 (47.6)	84 (62.2)	
Male	13 (26.5)	4 (66.7)	12 (31.6)	22 (52.4)	51 (37.8)	
Smoking, N (%)						0.329
Yes	8 (16.3)	0 (0.0)	12 (31.6)	7 (16.7)	27 (20.0)	
No	20 (40.8)	4 (66.7)	10 (26.3)	16 (38.1)	50 (37.0)	
Former	6 (12.2)	1 (16.7)	9 (23.7)	6 (14.3)	22 (16.3)	
Unknown	15 (30.6)	1 (16.7)	7 (18.4)	13 (31.0)	36 (26.7)	
Comorbidity, N (%)						0.237
No	6 (12.2)	0 (0.0)	2 (5.3)	1 (2.4)	9 (6.7)	
Yes	43 (87.8)	6 (100.0)	36 (94.7)	41 (97.6)	126 (93.3)	
Somatic comorbidity, N (%)						0.237
No	6 (12.2)	0 (0.0)	2 (5.3)	1 (2.4)	9 (6.7)	
Yes	43 (87.8)	6 (100.0)	36 (94.7)	41 (97.6)	126 (93.3)	
Psychiatric comorbidity, N (%)						0.096
No	45 (91.8)	6 (100.0)	29 (76.3)	38 (90.5)	118 (87.4)	
Yes	4 (8.2)	0 (0.0)	9 (23.7)	4 (9.5)	17 (12.6)	

Abbreviation: HYTILU, hypertensive ischemic leg ulceration.

### 3 | RESULTS

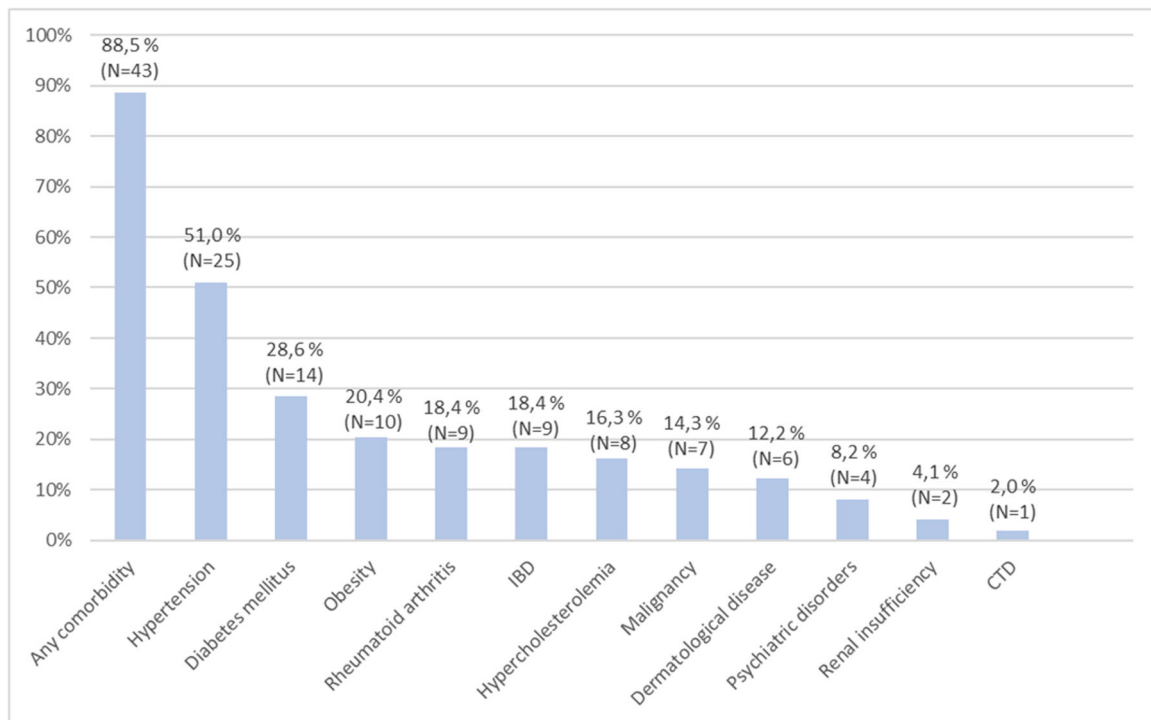
We found 135 cases with an atypical wound, which were more common in females ( $N = 84/135$ , 62.2%) than in males ( $N = 51$ , 37.8%) ( $p < 0.05$ ). The mean age at the time of diagnosis was 57.3 years for all cases. Those with PG (53.1) and factitious wound (53.0) were significantly younger than those with vasculitis (65.2) ( $p < 0.01$  and  $p > 0.05$ , respectively) (data not shown). Most cases ( $N = 126/135$ , 93.3%) had a comorbidity at the time of the diagnosis. Somatic diseases were diagnosed in 126 ( $N = 126/135$ , 93.3%) cases and psychiatric comorbidity was found in 17 ( $N = 17/135$ , 12.6%). Of the total study population, 27 ( $N = 27/135$ , 20.0%) smoked, 72 ( $n = 72/135$ , 53.3%) did not smoke or had quit, and 36 ( $N = 36/135$ , 26.7%) had an unknown tobacco background. The characteristics of the patients are presented in Table 1.

Most cases ( $N = 43/49$ , 87.8%) with PG had at least one comorbidity, with hypertension ( $N = 25/49$ , 51.0%) and diabetes mellitus ( $N = 14/49$ , 28.6%) being the most common ones (Figure 1), followed by inflammatory bowel diseases (IBDs) ( $N = 9/49$ , 18.4%) and rheumatoid arthritis (IRD) ( $N = 9/49$ , 18.4%). Three cases with PG

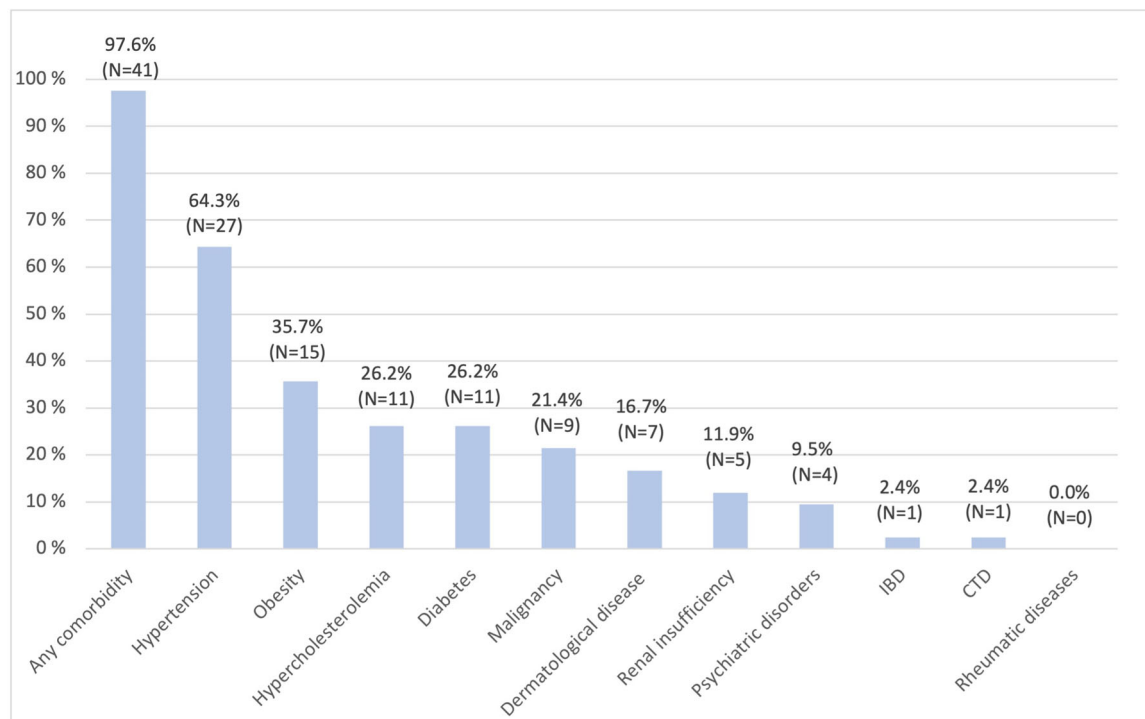
(6.1%) had depression and 1 (2.0%) had schizophrenia. Seven of the PG cases had malignancies (14.2%), of which four were hematological and three solid tumors.

All patients in the Martorell HYTILU/calciphylaxis group ( $N = 6$ ) had a diagnosis of hypertension and diabetes mellitus. Obesity ( $N = 4/6$ , 66.7%) and hypercholesterolemia ( $N = 3/6$ , 50.0%) were the next most common comorbidities. Among those with calciphylaxis, there was one case with renal insufficiency requiring dialysis treatment and three with warfarin medication. There were no cases with diagnosed malignancies or psychiatric disorders.

Almost every case ( $N = 41/42$ , 97.6%) with vasculitis ulcer had at least one comorbidity (Figure 2). The most common comorbidities were hypertension ( $N = 27/42$ , 64.3%), obesity ( $N = 15/42$ , 35.7%), hypercholesterolemia and diabetes ( $N = 11/42$ , 26.2% for both), and renal insufficiency ( $N = 5/42$ , 11.9%). Depression was seen in 7.1% ( $N = 3/42$ ) and one case had schizophrenia. As many as 16.7% ( $N = 7/42$ ) had other dermatological diseases, with eczemas ( $N = 4/42$ , 9.5%) being the most common. Every fifth case ( $N = 9/42$ , 21.4%) had a malignancy, most commonly a solid tumor. None were diagnosed with rheumatic diseases.



**FIGURE 1** Comorbidities of patients with pyoderma gangrenosum. CTD, connective tissue disease; IBD, inflammatory bowel disease (comprises ulcerative colitis and Crohn's disease).



**FIGURE 2** Comorbidities in patients diagnosed with vasculitis. CTD, connective tissue diseases; IBD, inflammatory bowel diseases (comprises ulcerative colitis and Crohn's disease).

Of the cases with factitious ulcer, 36 ( $N = 36/38$ , 94.7%) had at least one comorbidity. Hypertension ( $N = 15/38$ , 39.4%) and diabetes mellitus ( $N = 11/38$ , 28.9%) were most common comorbidities, followed by psychiatric disorders ( $N = 9/38$ , 23.7%), all of which were depression. One case had a malignancy and that was a solid tumor.

Overall, there were no statistically significant differences in the total somatic comorbidity between the patients with different types of wounds. However, psychiatric comorbidity was more often seen in patients with factitious wounds than in other groups, but it did not reach statistical significance (Table 1).

## 4 | DISCUSSION

In this study, we evaluated the clinical picture and comorbidities of 135 patients with atypical wounds based on the data from hospital patient records. There was a female predominance in the wounds. The most common type of atypical wound was PG, followed by vasculitis. The number of cases with factitious ulcers was surprisingly high. Almost every case had at least one comorbid disease and, or example, factitious wounds were commonly associated with psychiatric diseases.

The mean age of our patients was 57.3 years. In general, patients presenting with atypical wounds are younger than those with venous or arterial wounds.<sup>3</sup> All wounds are predominantly seen in adults; however, in rare cases, for example, PG can be seen in children as well.<sup>6</sup> In our study, there was only one PG adolescent case and none in children. In addition, subjects with PG or factitious wounds in the present study were younger than those with vasculitis or Martorell HYTILU/calciphylaxis, which is in line with previous studies.<sup>8</sup> The age of diagnosis varies in Martorell HYTILU, and some studies even suggest the mean age to be as high as 75 years old, but most commonly the patients are over 60 years of age<sup>8,11</sup> as in our study (63.2). In this study, the mean age of vasculitis patients was 65.2 years, which corresponds with previous reports.<sup>19</sup> Factitious wounds are usually seen in a younger population, most commonly in the late teens to early 20s.<sup>3,18</sup> In our study population, there were more older people with factitious ulcers (mean age 53.0); however, also one child was included.

In general, atypical wounds in the present study affected more females than males. In our study, PG was about three times more common in women than in men, which is in line with previous studies.<sup>3,6</sup> For factitious wounds, the female-to-male ratio varies from 3:1 to as high as 20:1 in the previous studies<sup>3</sup>; correspondingly, these wounds were more common in females in our study as well.

Based on previous studies, vasculitis and calciphylaxis are more commonly seen in women.<sup>14,20</sup> However, in our study vasculitis wounds predominated slightly in male patients, while calciphylaxis affected both sexes equally. Martorell HYTILU was seen more often in males in our study, whereas in recent studies the sex distribution in Martorell HYTILU has been reported to be similar in both sexes.<sup>16</sup> The female predominance among atypical wound patients can partly

derive from the fact that males in general are less likely to seek physician's help for their problems.<sup>21</sup>

The majority of our patients had at least one comorbid condition. In line with previous studies,<sup>17</sup> we found that subjects with PG had a high burden of inflammatory diseases since IBDs and IRD were found in almost every fifth case (18.4% for both). Although these prevalences are higher than in the Finnish general population (for IBD, 595 per 100,000 inhabitants and for IRD, 29.1 per 100,000),<sup>22,23</sup> a systematic review has reported IBD to be associated with up to 65% of PG cases.<sup>20</sup> Besides IBD and IRD, conditions such as hematological malignancies are common in PG patients.<sup>20</sup> This was also seen in our study population, since over half of the malignancies ( $N = 4/7$ ) in PG patients were hematological.

In our data, all the patients with Martorell HYTILU had both hypertension and diabetes mellitus as a comorbidity. Obesity was also common (66.7%). In line with other studies, hypertension has been reported to be present in 90%–100% and Type 2 diabetes in 40%–60% of patients with Martorell HYTILU.<sup>3,8</sup> It is thought that long-term hypertension with or without diabetes stimulates the ischemic arteriosclerosis of small subcutaneous vessels, which leads to the painful necrotic wounds typically seen in Martorell HYTILU.<sup>3,11</sup> It is well known that calciphylaxis is associated with chronic kidney diseases and especially with ESRD.<sup>8,24</sup> In addition, calciphylaxis can be warfarin-induced.<sup>21</sup> Thus, it is not surprising that also in our study, all cases with calciphylaxis had a history of either renal insufficiency or warfarin use.

Factitious wounds were also seen in surprisingly many and especially in young subjects in this study. In previous studies, the prevalence of factitious wounds has varied between 0.5% and 5% among selected patient groups. However, it is speculated that these wounds are more common than thought.<sup>25</sup> Differing markedly from other groups of atypical wounds in the present study, psychiatric comorbidities affected over 20% of the patients. In our patients, depression was the most typical psychiatric comorbidity, whereas other studies have more commonly reported personality disorders.<sup>3</sup>

The incidence of vasculitis has increased in recent decades, with it being now 3.9–4.5 per 100,000 individuals worldwide.<sup>12,13</sup> The majority of vasculitis show increasing incidence with age,<sup>13</sup> and with the aging of the population, it can be estimated that the number of vasculitis wounds will also rise. In this study, the most common comorbidities in patients with vasculitis were hypertension, diabetes mellitus, and obesity, as reported previously. In addition, there were five cases with simultaneous renal disease. An association between vasculitis and autoimmune disease such as lupus erythematosus or IRD has been reported,<sup>16</sup> but we found no cases with rheumatic diseases and only one (2.4%) case with connective tissue disease.

The major strength of this study was that all diagnoses were recorded in a tertiary care unit in the Department of Dermatology of the OUH by dermatologists. OUH is the only hospital with a department of dermatology in the Northern Ostrobothnia Hospital District providing special healthcare in dermatology for a Finnish

population of more than 413,000. Thus, the current study includes all the dermatological patients with atypical wounds treated in OUH between 1996 and 2019. There are some limitations in the study: In this retrospective study, data were based on patient records, and thus, there were some missing data concerning the history of smoking and comorbidities (some of them may be recorded in the general health care unit only). In addition, as an exact diagnosis code for Martorell HYTILU is still missing, it is possible that some of these wounds have not been reached by the selected ICD codes used in this study. Since the diagnosis of atypical wounds is challenging, we cannot exclude the possibility of misdiagnosis. Moreover, it was not possible to include wounds with neoplasm in the study because of the missing exact ICD code.

In conclusion, this study adds to the knowledge of the clinical picture and comorbidities of atypical wounds. Atypical wounds differ from other wounds: they affect more commonly young patients and can be associated with high comorbidity burden such as psychiatric diseases. Atypical wounds are characterized by specific sex distribution and, for example, PG and factitious wounds were seen more often in females than in males. Moreover, also the medication of patients with atypical wounds should be kept in mind; in our study, there were three subjects with calciphylaxis who had a history of warfarin use as an etiology of wounds. The diagnosis and treatment of atypical wounds are challenging and require a multidimensional approach. In many cases, the concomitant or associated disease or specific clinical characteristics can provide a clue for the diagnosis of the atypical wound.

#### AUTHOR CONTRIBUTIONS

**Jani Virkkala:** Writing—original draft. **Sara Polet:** Writing—original draft. **Jari Jokelainen:** Data curation; formal analysis; methodology; software; visualization. **Laura Huilaja:** Conceptualization; project administration; supervision; visualization; writing—review and editing. **Suvi-Päivikki Sinikumpu:** Conceptualization; project administration; supervision; writing—review and editing.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

#### DATA AVAILABILITY STATEMENT

Our data were retrieved from the OUH patient database. According to Finnish laws and regulations, the data in social welfare are confidential. The Medical Director of the Oulu University Hospital can, on a case-by-case basis, grant permission to use the registers and documents for purposes of scientific research. More information from research authorization applications can be found on [www.ppshp.fi](http://www.ppshp.fi). STROBE checklist has been followed when reporting the results of this study.

#### TRANSPARENCY STATEMENT

The lead author Suvi-Päivikki Sinikumpu affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted;

and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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