


Review

# SARS-CoV-2 vaccine-related cutaneous manifestations: a systematic review

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## Introduction

To date, over 250 million people have been reportedly infected by COVID-19 disease, which has spread across the globe, leading to approximately 5.1 million fatalities.<sup>1</sup> To prevent both COVID-19 and its viral transmission, DNA-based/RNA-based vaccines, non-replicating viral vector vaccines, and inactivated vaccines have been recently developed. Specifically, Pfizer-BioNTech, COVID-19 vaccine Moderna, Vaxzevria (previous COVID-19 vaccine AstraZeneca), and COVID-19 vaccine Johnson & Johnson (J&J)/Janssen have been currently authorized for use in the European Union by the European Medicines Agency (EMA). Other vaccines have been approved for use worldwide, including CoronaVac, an inactivated Chinese vaccine.<sup>2,3</sup> Although the above-mentioned vaccines are deemed to be generally safe, several side effects have been observed during clinical trials, encompassing a wide variety of vaccine-induced manifestations. Among these, skin and subcutaneous tissue

## Abstract

To date, over 250 million people have been reportedly infected by COVID-19 disease, which has spread across the globe and led to approximately 5.1 million fatalities. To prevent both COVID-19 and viral transmission, DNA-based/RNA-based vaccines, non-replicating viral vector vaccines, and inactivated vaccines have been recently developed. However, a precise clinical and histological characterization of SARS-CoV-2 vaccine-related dermatological manifestations is still lacking. A systematic review of 229 articles was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, in order to provide an extensive overview of SARS-CoV-2 vaccine-related skin manifestations. Data on demographics, number of reported cases with cutaneous involvement, vaccine, and rash type (morphology) were extracted from articles and summarized. A total of 5941 SARS-CoV-2 vaccine-related dermatological manifestations were gathered. Local injection-site reactions were the most frequently observed, followed by rash/unspecified cutaneous eruption, urticarial rashes, angioedema, herpes zoster, morbilliform/maculopapular/erythematous macular eruption, pityriasis rosea and pityriasis rosea-like eruptions, and other less common dermatological manifestations. Flares of pre-existing dermatological conditions were also reported. Cutaneous adverse reactions following SARS-CoV-2 vaccine administration seem to be heterogeneous, rather infrequent, and not life-threatening. Vaccinated patients should be monitored for skin manifestations, and dermatological evaluation should be offered, when needed.

disorders have been described with variable frequency, according to the type of vaccine administered, seemingly higher after vaccine Moderna. However, a precise clinical and histological characterization of SARS-CoV-2 vaccine-related dermatological manifestations is still lacking. Additionally, distinguishing between vaccine-related and unrelated cutaneous manifestations may be challenging. No large-scale studies have been conducted so far to determine the frequency and clinical features of these manifestations in real-life settings. Not surprisingly, since the introduction of vaccination programs worldwide, COVID-19 vaccine-related dermatological reactions have been increasingly reported: in this regard, dermatologists should be trained to promptly recognize these clinical manifestations, which should likely become common findings in their daily clinical practice.

Therefore, we conducted a systematic review aiming to provide an extensive overview of all the vaccine-related cutaneous manifestations reported in the literature thus far.

## Materials and methods

To shed light on the clinical features, differences, and potential mechanisms underlying SARS-CoV-2 vaccine-related dermatological manifestations, a systematic review was performed, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A search on MEDLINE, PubMed, Scopus, and Cochrane Library was conducted using the combination of the following keywords and medical subject heading (MeSH) terms: COVID vaccine, dermatology, rash, skin, cutaneous, BNT162, ChAdOX1, AstraZeneca, and mRNA-1273. The time range of our search was from March 1, 2020, to November 4, 2021. Only manuscripts in English were considered, and no restriction related to article type was applied; case reports, letters to the editor, case series, cross-sectional, and registry-based studies were all included. Studies were selected if they provided information on cutaneous manifestations reported after COVID-19 vaccine administration: patients receiving Pfizer-BioNTech, Moderna, J&J/Janssen, Covaxin, AstraZeneca, and CoronaVac vaccines, both first and second doses, were included. Patients experiencing a flare of a pre-existing skin condition were also included. Reviews, position paper, or publications reporting suspected SARS-CoV-2 vaccine-related cutaneous manifestations categorized as “unlikely” (score range from -4 to 0) according to the adverse drug reaction probability scale of Naranjo *et al.*<sup>4</sup> were excluded. Two authors (GA and GR) independently assessed the risk of bias of each included study, in accordance with methods recommended by the National Institutes of Health Quality Assessment Tool for Case Series Studies.<sup>5</sup> Authors resolved disagreements by consensus-based discussion, and a third author (FC) was consulted to resolve disagreements when required. In cases where the same sample was used for more than one study, all studies were reviewed to determine the extent to which there may be duplication in the reported outcomes between studies. The full text of selected studies was reviewed, and data on demographics, article type, number of reported cases with cutaneous involvement, vaccine, and rash type (morphology) were extracted from articles texts, tables, figures, and summarized through a descriptive table (Table 1)<sup>6-234</sup> and narrative discussion.

## Results

A total of 1549 records were initially identified through a literature search, 477 of which were duplicates. After screening for eligibility and inclusion criteria, 229 articles were ultimately included (Fig. 1). Most publications were letters to the editor ( $n = 117$ ), followed by case reports ( $n = 51$ ), correspondences ( $n = 23$ ), case series ( $n = 16$ ), original articles ( $n = 16$ ), commentaries ( $n = 3$ ), and clinical images ( $n = 3$ ). All the studies included were rated as level 4 or 5 evidence for clinical research as detailed in the Oxford Centre for Evidence-Based Medicine 2011 guidelines.<sup>235</sup> A total

of 4649 patients with SARS-CoV-2 vaccine-related dermatological manifestations were gathered.

Some patients experienced more than one cutaneous manifestation, either after the first or the second dose. Various cutaneous manifestations have been described, for a total of 5941 cases. The most frequent were local injection-site reactions ( $n = 2023$ ), followed by rash or unspecified cutaneous eruption ( $n = 1954$ ), urticaria ( $n = 647$ ), angioedema ( $n = 318$ ), herpes zoster ( $n = 160$ ), morbilliform/maculopapular/erythematous macular eruption ( $n = 106$ ), pityriasis rosea/pityriasis rosea-like ( $n = 96$ ), vesicular/papulovesicular rash ( $n = 53$ ), chilblains-like/pernio ( $n = 52$ ), purpuric rash/vasculitis ( $n = 46$ ), flushing ( $n = 41$ ), new onset of autoimmune blistering disease ( $n = 37$ ), flare of psoriasis ( $n = 36$ ), flare of pre-existing non-specified dermatological condition ( $n = 34$ ), erythema multiforme/multiforme like ( $n = 33$ ), erythema ( $n = 25$ ), new onset/flare of eczema ( $n = 25$ ), delayed inflammatory reaction to dermal hyaluronic acid filler ( $n = 23$ ), flare of atopic dermatitis ( $n = 20$ ), erythromelalgia ( $n = 19$ ), skin discoloration ( $n = 15$ ), contact dermatitis ( $n = 15$ ), petechial rash ( $n = 10$ ), fixed drug eruption ( $n = 8$ ), flare of autoimmune blistering disease ( $n = 8$ ), herpes simplex ( $n = 8$ ), alopecia ( $n = 7$ ), new onset of cutaneous lupus erythematosus ( $n = 6$ ), and neutrophilic dermatosis/Sweet syndrome ( $n = 6$ ). Less common skin manifestations (i.e., less than six reported cases) are summarized in Table 1. Herein we provide a comprehensive overview of the most frequently observed skin-related manifestation following SARS-CoV-2 vaccine administration (Table 1, Fig. 2) and describe the potential mechanisms underlying their development.

### Local injection-site reactions

Local injection-site reactions (immediate or delayed) ( $n = 2023$ ) have been the most common SARS-CoV-2 vaccine-related dermatological manifestations. Notably, Moderna seemed to be the vaccine relatively most frequently leading to this type of reaction, having been administered in a total of 1607 (79.43%) cases of out 2023 reporting it. Reasons why the Moderna vaccine more frequently induced skin-related manifestations compared to the Pfizer-BioNTech mRNA vaccine are unknown, and further studies are needed to clarify it.

The largest cohort of patients has been collected by McMahon *et al.*<sup>138</sup> ( $n = 1104$ ). They developed local injection-site reactions most frequently 1–5 days following Moderna vaccine ( $n = 983$ ) or after Pfizer-BioNTech COVID-19 vaccine ( $n = 103$ ).

A clinicopathological study of a delayed-type hypersensitivity reaction following Moderna vaccine revealed as main features focal epidermal changes with epidermal spongiosis and exocytosis of a few lymphocytes as well as a perivascular and occasionally sleeve-like inflammatory infiltrate predominantly composed of small lymphocytes with an admixture of a variable number of eosinophilic granulocytes in the dermis.<sup>84</sup>

Whether local injection-site manifestation corresponds to a hypersensitivity reaction to the spike protein or to different components of the vaccine is still unclear. As far as it

**Table 1** Overview of SARS-CoV-2 vaccine-related cutaneous manifestations reported in the literature

SARS-CoV-2 vaccine-related dermatological manifestations	Number of cases (N = 5941) (100%)	Cases reported by vaccine type* (publication's first author)	Overall reported cases by vaccine type (if available)
Local injection-site reactions (immediate/delayed)	2023 (34.05%)	4 Moderna (Wei <i>et al.</i> <sup>10</sup> ), 103 Pfizer (Fernandez-Nieto <i>et al.</i> <sup>12</sup> ), 17 Pfizer (Farinazzo <i>et al.</i> <sup>235</sup> ), 3 Pfizer (Corbeddu <i>et al.</i> <sup>14</sup> ), 983 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 103 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 2 JJ (McMahon <i>et al.</i> <sup>138</sup> ), 9 Astrazeneca (McMahon <i>et al.</i> <sup>138</sup> ), 7 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 1 Pfizer (Lopez-Valle <i>et al.</i> <sup>17</sup> ), 16 Moderna (Johnston <i>et al.</i> <sup>38</sup> ), 1 Pfizer (Gyldenløve <i>et al.</i> <sup>39</sup> ), 3 Pfizer (Tammaro <i>et al.</i> <sup>45</sup> ), 13 Moderna (Jacobson <i>et al.</i> <sup>54</sup> ), 1 Pfizer (Edriss <i>et al.</i> <sup>58</sup> ), 4 Astrazeneca (Kim <i>et al.</i> <sup>65</sup> ), 1 Moderna (Mahmood <i>et al.</i> <sup>74</sup> ), 3 Moderna (Kempf <i>et al.</i> <sup>84</sup> ), 1 Moderna (Larson <i>et al.</i> <sup>92</sup> ), 1 Pfizer (Larson <i>et al.</i> <sup>92</sup> ), 84 Moderna (Papadimitriou <i>et al.</i> <sup>91</sup> ), 1 Pfizer (Gregoriou <i>et al.</i> <sup>125</sup> ), 3 Moderna (Gregoriou <i>et al.</i> <sup>125</sup> ), 11 Moderna (Hoff <i>et al.</i> <sup>129</sup> ), 1 Moderna (Tihy <i>et al.</i> <sup>130</sup> ), 1 Pfizer (Choi <i>et al.</i> <sup>135</sup> ), 12 Pfizer (Vaccaro <i>et al.</i> <sup>146</sup> ), 16 Astrazeneca (Vaccaro <i>et al.</i> <sup>146</sup> ), 5 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 4 Astrazeneca (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ), 1 Moderna (Guénin <i>et al.</i> <sup>183</sup> ), 1 Pfizer (Zengarini <i>et al.</i> <sup>182</sup> ), 2 Moderna (Papamanoli <i>et al.</i> <sup>184</sup> ), 12 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 459 Moderna (Samarakoon <i>et al.</i> <sup>197</sup> ), 35 Pfizer (Samarakoon <i>et al.</i> <sup>197</sup> ), 16 Not specified (Samarakoon <i>et al.</i> <sup>197</sup> ), 1 Astrazeneca (Sprute <i>et al.</i> <sup>199</sup> ), 1 Moderna (Saifuddin <i>et al.</i> <sup>201</sup> ), 8 Astrazeneca (Yu <i>et al.</i> <sup>204</sup> ), 1 Pfizer (Fata <i>et al.</i> <sup>213</sup> ), 44 Pfizer (Riad <i>et al.</i> <sup>210,233</sup> ), 2 Pfizer (Sato <i>et al.</i> <sup>216</sup> ), 3 Moderna (Sato <i>et al.</i> <sup>216</sup> ), 21 Moderna (Juarez Guerrero <i>et al.</i> <sup>230</sup> ), 1 Pfizer (Juarez Guerrero <i>et al.</i> <sup>230</sup> ).	Pfizer: 332 Astrazeneca: 42 Moderna: 1607 JJ: 2 Coronavac: 5 Not Specified: 35
Rash/Unspecified cutaneous eruption	1954 (32.88%)	5 Pfizer (Fernandez-Nieto <i>et al.</i> <sup>12</sup> ), 2 Pfizer (Farinazzo <i>et al.</i> <sup>234</sup> ), 2 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 2 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 58 Not specified (Kadali <i>et al.</i> <sup>34</sup> ), 37 Pfizer (Riad <i>et al.</i> <sup>233</sup> ), 1 JJ (Lospinoso <i>et al.</i> <sup>48</sup> ), 1 Pfizer (Larson <i>et al.</i> <sup>92</sup> ), 3 Pfizer (Pasternack <i>et al.</i> <sup>89</sup> ), 1 Astrazeneca (Annabi <i>et al.</i> <sup>108</sup> ), 10 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 97 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 108 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 19 Astrazeneca (Rerknimitr <i>et al.</i> <sup>175</sup> ), 14 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 1 Pfizer (Zafar <i>et al.</i> <sup>185</sup> ), 1 Astrazeneca (Zafar <i>et al.</i> <sup>185</sup> ), 1 Pfizer (Irvine <i>et al.</i> <sup>191</sup> ), 11 Not specified (Samarakoon <i>et al.</i> <sup>197</sup> ), 8 Astrazeneca (Riad <i>et al.</i> <sup>202</sup> ), 12 Not specified (Klugar <i>et al.</i> <sup>206</sup> ), 5 Astrazeneca (Klugar <i>et al.</i> <sup>206</sup> ), 8 Pfizer (Riad <i>et al.</i> <sup>210,212</sup> ), 1 Pfizer (Al-ansari <i>et al.</i> <sup>226</sup> ), 307 Astrazeneca (Al Bahrani <i>et al.</i> <sup>228</sup> ), 11 Pfizer (Bookstein Peretz <i>et al.</i> <sup>227</sup> ), 2 Moderna (Juarez Guerrero <i>et al.</i> <sup>230</sup> ), 245 Pfizer (Robinson <i>et al.</i> <sup>231</sup> ), 981 Moderna (Robinson <i>et al.</i> <sup>231</sup> ).	Pfizer: 317 Astrazeneca: 341 Moderna: 985 JJ: 1 Coronavac: 118 Not Specified: 192
Urticaria	647 (10.89%)	2 Pfizer (Fernandez-Nieto <i>et al.</i> <sup>12</sup> ), 10 Pfizer (Farinazzo <i>et al.</i> <sup>235</sup> ), 2 Pfizer (Bianchi <i>et al.</i> <sup>13</sup> ), 1 Pfizer (Corbeddu <i>et al.</i> <sup>14</sup> ), 48 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 40 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 7 Not specified (Kadali <i>et al.</i> <sup>34</sup> ), 7 Pfizer (Riad <i>et al.</i> <sup>233</sup> ), 6 Moderna (Sidlow <i>et al.</i> <sup>55</sup> ), 1 Pfizer (Patruno <i>et al.</i> <sup>62</sup> ), 1 Astrazeneca (Baraldi <i>et al.</i> <sup>93</sup> ), 4 Coronavac (Akdas <i>et al.</i> <sup>112</sup> ), 12 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 1 Moderna (Holmes <i>et al.</i> <sup>124</sup> ), 2 Pfizer (Choi <i>et al.</i> <sup>135</sup> ), 7 Coronavac (Triwatcharikorn <i>et al.</i> <sup>167</sup> ), 2 Pfizer (Peigottu <i>et al.</i> <sup>158</sup> ), 92 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 12 Astrazeneca (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ), 1 Astrazeneca (Niebel <i>et al.</i> <sup>179</sup> ), 1 Astrazeneca (Burlando <i>et al.</i> <sup>181</sup> ), 2 Coronavac (Yu <i>et al.</i> <sup>204</sup> ), 1 Astrazeneca (Yu <i>et al.</i> <sup>204</sup> ), 2 Astrazeneca (Klugar <i>et al.</i> <sup>206</sup> ), 2 Not specified (Klugar <i>et al.</i> <sup>206</sup> ), 4 Not specified (Riad <i>et al.</i> <sup>233</sup> ), 55 Pfizer (Robinson <i>et al.</i> <sup>231</sup> ), 321 Moderna (Robinson <i>et al.</i> <sup>231</sup> ).	Pfizer: 123 Astrazeneca: 18 Moderna: 376 Coronavac: 117 Not Specified: 13
Angioedema	318 (5.35%)	2 Pfizer (Farinazzo <i>et al.</i> <sup>235</sup> ), 2 Pfizer (Bianchi <i>et al.</i> <sup>13</sup> ), 10 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 2 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 Astrazeneca (McMahon <i>et al.</i> <sup>138</sup> ), 2 Coronavac (Akdas <i>et al.</i> <sup>112</sup> ), 3 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 1 Moderna (Holmes <i>et al.</i> <sup>124</sup> ), 2 Pfizer (Peigottu <i>et al.</i> <sup>158</sup> ), 9 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 3 Coronavac (Yu <i>et al.</i> <sup>204</sup> ), 2 Astrazeneca (Yu <i>et al.</i> <sup>204</sup> ), 2 Not specified (Klugar <i>et al.</i> <sup>206</sup> ), 2 Astrazeneca (Klugar <i>et al.</i> <sup>206</sup> ), 13 Pfizer (Riad <i>et al.</i> <sup>210</sup> ), 1 Moderna (Juarez Guerrero <i>et al.</i> <sup>230</sup> ), 34 Pfizer (Robinson <i>et al.</i> <sup>231</sup> ), 227 Moderna (Robinson <i>et al.</i> <sup>231</sup> ).	Pfizer: 55 Astrazeneca: 5 Moderna: 239 Coronavac: 17 Not Specified: 2

Table 1 Continued

SARS-CoV-2 vaccine-related dermatological manifestations	Number of cases (N = 5941) (100%)	Cases reported by vaccine type* (publication's first author)	Overall reported cases by vaccine type (if available)
Herpes zoster	160 (2.69%)	2 Pfizer (Farinazzo <i>et al.</i> <sup>234</sup> ), 1 Pfizer (Burlando <i>et al.</i> <sup>11</sup> ), 24 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 22 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 JJ (McMahon <i>et al.</i> <sup>138</sup> ), 5 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 1 Coronavac (Bostan <i>et al.</i> <sup>7</sup> ), 1 Pfizer (Eid <i>et al.</i> <sup>24</sup> ), 5 Pfizer (Rodríguez-Jiménez <i>et al.</i> <sup>29</sup> ), 14 Moderna (Lee <i>et al.</i> <sup>41</sup> ), 6 Pfizer (Lee <i>et al.</i> <sup>41</sup> ), 1 Pfizer (Tessas <i>et al.</i> <sup>49</sup> ), 2 Pfizer (Alpalhão <i>et al.</i> <sup>96</sup> ), 2 Astrazeneca (Alpalhão <i>et al.</i> <sup>96</sup> ), 6 Pfizer (Furer <i>et al.</i> <sup>95</sup> ), 1 Moderna (Channa <i>et al.</i> <sup>105</sup> ), 2 Coronavac (Özdemir <i>et al.</i> <sup>111</sup> ), 2 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 3 Covishield (Mohta <i>et al.</i> <sup>139</sup> ), 19 Pfizer (Fathy <i>et al.</i> <sup>136</sup> ), 16 Moderna (Fathy <i>et al.</i> <sup>136</sup> ), 4 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 1 Covishield (Mehta <i>et al.</i> <sup>151</sup> ), 2 Pfizer (Kluger <i>et al.</i> <sup>176</sup> ), 2 Astrazeneca (Kluger <i>et al.</i> <sup>176</sup> ), 2 Pfizer (van Dam <i>et al.</i> <sup>194</sup> ), 2 Covishield (Palanivel <i>et al.</i> <sup>196</sup> ), 1 Astrazeneca (Ardalan <i>et al.</i> <sup>211</sup> ), 1 Pfizer (Sato <i>et al.</i> <sup>216</sup> ), 8 Pfizer (Koumaki <i>et al.</i> <sup>221</sup> ), 1 Astrazeneca (Koumaki <i>et al.</i> <sup>221</sup> ), 1 Moderna (David <i>et al.</i> <sup>229</sup> ), 1 Covaxin (Arora <i>et al.</i> <sup>232</sup> ).	Pfizer: 78 Astrazeneca: 6 Moderna: 56 JJ: 1 Coronavac: 5 Covishield: 4 Covaxin: 1 Not Specified: 9
Morbilliform/Maculopapular/Erythematous macular eruption	106 (1.78%)	1 Pfizer (Jedlowski <i>et al.</i> <sup>9</sup> ), 2 Pfizer (Farinazzo <i>et al.</i> <sup>234</sup> ), 42 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 23 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 JJ (McMahon <i>et al.</i> <sup>138</sup> ), 1 Astrazeneca (McMahon <i>et al.</i> <sup>138</sup> ), 3 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 1 Pfizer (Ackerman <i>et al.</i> <sup>32</sup> ), 1 Pfizer (Rojas-Pérez-Ezquerre <i>et al.</i> <sup>35</sup> ), 1 Pfizer (Ohsawa <i>et al.</i> <sup>66</sup> ), 1 Moderna (Larson <i>et al.</i> <sup>92</sup> ), 2 Pfizer (Annabi <i>et al.</i> <sup>108</sup> ), 1 Moderna (Holmes <i>et al.</i> <sup>124</sup> ), 1 Pfizer (Tihy <i>et al.</i> <sup>130</sup> ), 5 Pfizer (Peigottu <i>et al.</i> <sup>158</sup> ), 5 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Astrazeneca (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 2 Pfizer (Nanamori <i>et al.</i> <sup>189</sup> ), 3 Coronavac (Yu <i>et al.</i> <sup>204</sup> ), 1 Astrazeneca (Yu <i>et al.</i> <sup>204</sup> ), 2 Moderna (Juarez Guerrero <i>et al.</i> <sup>230</sup> ), 5 Pfizer (Juarez Guerrero <i>et al.</i> <sup>230</sup> ).	Pfizer: 44 Astrazeneca: 3 Moderna: 46 JJ: 1 Coronavac: 8 Not Specified: 4
Pityriasis rosea/Pityriasis rosea-like	96 (1.62%)	2 Pfizer (Farinazzo <i>et al.</i> <sup>234</sup> ), 13 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 6 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 2 Astrazeneca (McMahon <i>et al.</i> <sup>138</sup> ), 3 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 2 Pfizer (Busto-Leis <i>et al.</i> <sup>20</sup> ), 1 Pfizer (Carballido-Vázquez <i>et al.</i> <sup>22</sup> ), 1 Coronavac (Akdas <i>et al.</i> <sup>26</sup> ), 2 Pfizer (Cyrenne <i>et al.</i> <sup>40</sup> ), 1 Pfizer (Abdullah <i>et al.</i> <sup>56</sup> ), 1 Covishield (Adya <i>et al.</i> <sup>64</sup> ), 2 Pfizer (Marcantonio-Santa Cruz <i>et al.</i> <sup>82</sup> ), 1 Moderna (Larson <i>et al.</i> <sup>92</sup> ), 14 Pfizer (Temiz <i>et al.</i> <sup>110</sup> ), 17 Coronavac (Temiz <i>et al.</i> <sup>110</sup> ), 1 Coronavac (Akdas <i>et al.</i> <sup>112</sup> ), 8 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 1 Pfizer (Cohen <i>et al.</i> <sup>128</sup> ), 1 Pfizer (Tihy <i>et al.</i> <sup>130</sup> ), 1 Pfizer (Choi <i>et al.</i> <sup>135</sup> ), 2 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 1 Covishield (Mehta <i>et al.</i> <sup>151</sup> ), 1 Astrazeneca (Leerunyakul <i>et al.</i> <sup>156</sup> ), 1 Not specified (Bostan <i>et al.</i> <sup>160</sup> ), 2 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Pfizer (Niegel <i>et al.</i> <sup>179</sup> ), 1 Astrazeneca (Niegel <i>et al.</i> <sup>179</sup> ), 3 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 1 Astrazeneca (Yu <i>et al.</i> <sup>204</sup> ), 1 Astrazeneca (Pedrazini <i>et al.</i> <sup>208</sup> ), 2 Not specified (Huang <i>et al.</i> <sup>218</sup> ).	Pfizer: 34 Astrazeneca: 6 Moderna: 14 Coronavac: 29 Covishield: 2 Not Specified: 11
Vesicular/Papulovesicular rash	53 (0.89%)	22 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 19 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 Astrazeneca (Tammamo <i>et al.</i> <sup>36</sup> ), 6 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Astrazeneca (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Pfizer (Niegel <i>et al.</i> <sup>179</sup> ), 1 Not specified (Niegel <i>et al.</i> <sup>179</sup> ), 1 Pfizer (Santovito <i>et al.</i> <sup>186</sup> ), 1 Coronavac (Yu <i>et al.</i> <sup>204</sup> ).	Pfizer: 21 Astrazeneca: 2 Moderna: 22 Coronavac: 7 Not Specified: 1
Chilblains-like/Pernio	52 (0.88%)	1 Pfizer (Farinazzo <i>et al.</i> <sup>234</sup> ), 3 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 5 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 Pfizer (Lopez <i>et al.</i> <sup>18</sup> ), 1 Moderna (Kha <i>et al.</i> <sup>19</sup> ), 2 Coronavac (Temiz <i>et al.</i> <sup>21</sup> ), 1 Pfizer (Piccolo <i>et al.</i> <sup>27</sup> ), 1 Pfizer (Lesort <i>et al.</i> <sup>60</sup> ), 1 Moderna (Kelso <i>et al.</i> <sup>63</sup> ), 3 Moderna (Revilla-Nebreda <i>et al.</i> <sup>100</sup> ), 1 Pfizer (Cameli <i>et al.</i> <sup>83</sup> ), 1 Pfizer (Annabi <i>et al.</i> <sup>108</sup> ), 1 Pfizer (Souaid <i>et al.</i> <sup>114</sup> ), 1 Moderna (Holmes <i>et al.</i> <sup>124</sup> ), 11 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 4 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 12 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 1 Pfizer (Qiao <i>et al.</i> <sup>209</sup> ).	Pfizer: 25 Moderna: 20 Coronavac: 2 Not Specified: 5
Purpuric rash/New onset or flare of vasculitis	46 (0.77%)	2 Pfizer (Lam <i>et al.</i> <sup>15</sup> ), 3 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 5 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 Pfizer (Cohen <i>et al.</i> <sup>128</sup> ), 1 Moderna (Malayala <i>et al.</i> <sup>33</sup> ), 3 Pfizer (Mazzatenta <i>et al.</i> <sup>47</sup> ), 1 Pfizer (Krajewski <i>et al.</i> <sup>51</sup> ), 1 Covaxin (Kharkar <i>et al.</i> <sup>57</sup> ), 1 Pfizer (Falkenhain-López <i>et al.</i> <sup>79</sup> ), 1 Pfizer (Nastro <i>et al.</i> <sup>98</sup> ), 1	Pfizer: 21 Astrazeneca: 6 Moderna: 4 Covaxin: 2

**Table 1 Continued**

SARS-CoV-2 vaccine-related dermatological manifestations	Number of cases (N = 5941) (100%)	Cases reported by vaccine type* (publication's first author)	Overall reported cases by vaccine type (if available)
		Coronavac (Bostan <i>et al.</i> <sup>85</sup> ), 1 Astrazeneca (Guzmán-Pérez <i>et al.</i> <sup>101</sup> ), 1 Pfizer (Vassallo <i>et al.</i> <sup>104</sup> ), 1 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 1 Pfizer (Mücke <i>et al.</i> <sup>143</sup> ), 1 Covishield (Sandhu <i>et al.</i> <sup>147</sup> ), 1 Covaxin (Kar <i>et al.</i> <sup>140</sup> ), 2 Coronavac (Bencharattanaphakhi <i>et al.</i> <sup>173</sup> ), 8 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 3 Astrazeneca (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ), 1 Pfizer (Cazzato <i>et al.</i> <sup>187</sup> ), 1 Astrazeneca (Yu <i>et al.</i> <sup>204</sup> ), 1 Pfizer (King <i>et al.</i> <sup>215</sup> ), 1 Pfizer (Hines <i>et al.</i> <sup>214</sup> ), 1 Pfizer (Iwata <i>et al.</i> <sup>219</sup> ), 1 Astrazeneca (Jin <i>et al.</i> <sup>222</sup> ).	Coronavac: 12 Covishield: 1
Flushing	41 (0.69%)	2 Pfizer (Bianchi <i>et al.</i> <sup>13</sup> ), 39 Not specified (Kadali <i>et al.</i> <sup>34</sup> ).	Pfizer: 2 Not Specified: 39
New onset of autoimmune blistering disease	37 (0.62%)	1 Pfizer (Solimani <i>et al.</i> <sup>68</sup> ), 4 Pfizer (Coto-Segura <i>et al.</i> <sup>77</sup> ), 8 Pfizer (Tomayko <i>et al.</i> <sup>88</sup> ), 4 Moderna (Tomayko <i>et al.</i> <sup>88</sup> ), 1 Moderna (Larson <i>et al.</i> <sup>92</sup> ), 1 Pfizer (Larson <i>et al.</i> <sup>92</sup> ), 5 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 10 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 Pfizer (Young <i>et al.</i> <sup>153</sup> ), 1 Moderna (Khalid <i>et al.</i> <sup>188</sup> ), 1 Pfizer (Nakamura <i>et al.</i> <sup>220</sup> ).	Pfizer: 26 Moderna: 11
Flare of psoriasis	36 (0.61%)	1 Pfizer (Krajewski <i>et al.</i> <sup>59</sup> ), 1 Pfizer (Mieczkowska <i>et al.</i> <sup>75</sup> ), 1 Pfizer (Quattrini <i>et al.</i> <sup>81</sup> ), 1 Covishield (Nagrani <i>et al.</i> <sup>106</sup> ), 7 Astrazeneca (Sotiriou <i>et al.</i> <sup>113</sup> ), 1 Moderna (Sotiriou <i>et al.</i> <sup>113</sup> ), 6 Pfizer (Sotiriou <i>et al.</i> <sup>113</sup> ), 1 Pfizer (Bostan <i>et al.</i> <sup>126</sup> ), 1 Coronavac (Bostan <i>et al.</i> ), 2 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 3 Astrazeneca (Megna <i>et al.</i> <sup>142</sup> ), 1 Moderna (Megna <i>et al.</i> <sup>142</sup> ), 7 Pfizer (Megna <i>et al.</i> <sup>142</sup> ), 1 Moderna (Pesqué <i>et al.</i> <sup>154</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ), 1 Astrazeneca (Fang <i>et al.</i> <sup>217</sup> ).	Pfizer: 18 Astrazeneca: 11 Moderna: 3 Covishield: 1 Coronavac: 1 Not Specified: 2
Flare of pre-existing non-specified dermatological condition	34 (0.57%)	4 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 11 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 19 Not specified (McMahon <i>et al.</i> <sup>138</sup> ).	Pfizer: 11, Moderna: 4 Not Specified: 19
Erythema Multiforme/ Multiforme like	33 (0.57%)	16 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 3 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 Pfizer (Lavery <i>et al.</i> <sup>25</sup> ), 1 Pfizer (Patruno <i>et al.</i> ), 1 Coronavac (Akdas <i>et al.</i> <sup>112</sup> ), 1 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 1 Pfizer (Buján Bonino <i>et al.</i> <sup>133</sup> ), 1 Pfizer (Scharf <i>et al.</i> <sup>155</sup> ), 1 Pfizer (Borg <i>et al.</i> <sup>148</sup> ), 1 Pfizer (de las Vecillas <i>et al.</i> <sup>163</sup> ), 1 Pfizer (Sechi <i>et al.</i> <sup>169</sup> ), 1 Pfizer (Kim <i>et al.</i> <sup>177</sup> ), 3 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 1 Moderna (Saibene <i>et al.</i> <sup>203</sup> )	Pfizer: 11 Moderna: 17 Coronavac: 2 Not Specified: 3
Erythema	25 (0.42%)	6 Pfizer (Farinazzo <i>et al.</i> <sup>234</sup> ), 7 Pfizer (Corbeddu <i>et al.</i> <sup>14</sup> ), 2 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 2 Pfizer (Tihy <i>et al.</i> <sup>130</sup> ), 1 Moderna (Tihy <i>et al.</i> <sup>130</sup> ), 2 Not Specified (McMahon <i>et al.</i> <sup>138</sup> ), 4 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 1 Pfizer (Nune <i>et al.</i> <sup>225</sup> ).	Pfizer: 16 Moderna: 1 Coronavac: 2 Not Specified: 6
New onset/Flare of eczema	25 (0.42%)	1 Pfizer (Holmes <i>et al.</i> <sup>124</sup> ), 2 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 4 Astrazeneca (Rerknimitr <i>et al.</i> <sup>175</sup> ), 17 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ).	Pfizer: 1 Astrazeneca: 4 Coronavac: 17 Not Specified: 3
Delayed inflammatory reaction to dermal hyaluronic acid filler	23 (0.39%)	14 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 2 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 2 Pfizer (Munavalli <i>et al.</i> <sup>31</sup> ), 2 Moderna (Munavalli <i>et al.</i> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 2 Pfizer (Michon <i>et al.</i> <sup>205</sup> ).	Pfizer: 6 Moderna: 16 Not Specified: 1
Flare of atopic dermatitis	20 (0.34)	4 Not specified (Kadali <i>et al.</i> <sup>34</sup> ), 2 Pfizer (Leasure <i>et al.</i> <sup>80</sup> ), 1 Pfizer (Larson <i>et al.</i> <sup>92</sup> ), 1 Moderna (Larson <i>et al.</i> <sup>92</sup> ), 1 Pfizer (Bekkali <i>et al.</i> <sup>89</sup> ), 8 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 2 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ).	Pfizer: 5 Moderna: 1 Coronavac: 8 Not Specified: 6
Erythromelalgia	19 (0.32%)	14 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 5 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ).	Pfizer: 5 Moderna: 14 Not Specified: 15
Skin discoloration	15 (0.25%)	15 Not specified (Kadali <i>et al.</i> <sup>34</sup> ).	Not Specified: 15
Contact dermatitis	15 (0.25%)	7 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 5 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 3 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ).	Pfizer: 8 Moderna: 7
Petechial rash	10 (0.17%)	1 Coronavac (Cebeci <i>et al.</i> <sup>44</sup> ), 4 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 3 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 1 Astrazeneca (Waraich <i>et al.</i> <sup>193</sup> ), 1 Coronavac (Yu <i>et al.</i> <sup>204</sup> ).	Pfizer: 3 Astrazeneca: 1 Moderna: 4 Coronavac: 2

Table 1 Continued

SARS-CoV-2 vaccine-related dermatological manifestations	Number of cases (N = 5941) (100%)	Cases reported by vaccine type* (publication's first author)	Overall reported cases by vaccine type (if available)
Fixed drug eruption	8 (0.13%)	1 Pfizer (Farinazzo <i>et al.</i> <sup>234</sup> ), 1 Pfizer (Mintoff <i>et al.</i> <sup>46</sup> ), 1 Moderna (Annabi <i>et al.</i> <sup>108</sup> ), 2 Not specified (McMahon <i>et al.</i> <sup>138</sup> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ), 2 Moderna (Juarez Guerrero <i>et al.</i> <sup>230</sup> ).	Pfizer: 2 Moderna: 3 Not Specified: 3
Flare of autoimmune blistering disease	8 (0.13%)	3 Moderna (Damiani <i>et al.</i> <sup>67</sup> ), 2 Pfizer (Damiani <i>et al.</i> <sup>67</sup> ), 1 Pfizer (Tomayko <i>et al.</i> <sup>88</sup> ), 2 Not specified (McMahon <i>et al.</i> <sup>138</sup> ).	Pfizer: 3 Moderna: 3 Not Specified: 2
Herpes simplex	8 (0.13%)	2 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 4 Pfizer (Fathy <i>et al.</i> <sup>136</sup> ), 1 Moderna (Fathy <i>et al.</i> <sup>136</sup> ), 1 Pfizer (Kluger <i>et al.</i> ).	Pfizer: 5 Moderna: 1 Coronavac: 2
Alopecia	7 (0.12%)	2 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 2 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ), 2 JJ (McMahon <i>et al.</i> <sup>138</sup> ), 1 Astrazeneca (Essam <i>et al.</i> <sup>157</sup> ).	Pfizer: 2 Moderna: 2 Astrazeneca: 1 JJ: 2
New onset cutaneous lupus erythematosus	6 (0.10%)	1 Pfizer (Kreuter <i>et al.</i> <sup>90</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ), 2 Moderna (Niebel <i>et al.</i> <sup>179</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>223</sup> ), 1 Moderna (Niebel <i>et al.</i> <sup>223</sup> ).	Pfizer: 3 Moderna: 3
Neutrophilic dermatosis/Sweet syndrome	6 (0.10%)	1 Pfizer (Darrigade <i>et al.</i> <sup>61</sup> ), 1 Astrazeneca (Capassoni <i>et al.</i> <sup>71</sup> ), 1 Moderna (Torrealba-Acosta <i>et al.</i> <sup>102</sup> ), 1 Astrazeneca (Sechi <i>et al.</i> <sup>169</sup> ), 1 Covishield (Majid <i>et al.</i> <sup>162</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ).	Pfizer: 2 Astrazeneca: 2 Moderna: 1 Covishield: 1
Pityriasis rubra pilaris	5 (0.08%)	1 Astrazeneca (Lladó <i>et al.</i> <sup>103</sup> ), 1 Pfizer (Hunjan <i>et al.</i> <sup>117</sup> ), 1 Covishield (Sahni <i>et al.</i> <sup>122</sup> ), 1 Moderna (Sechi <i>et al.</i> <sup>169</sup> ), 1 Pfizer (Sechi <i>et al.</i> <sup>169</sup> ).	Pfizer: 2 Moderna: 1 Astrazeneca: 1 Covishield: 1
Flare of lichen planus	5 (0.08%)	1 Pfizer (Hiltun <i>et al.</i> <sup>8</sup> ), 4 Not specified (McMahon <i>et al.</i> <sup>138</sup> ).	Pfizer: 1 Not Specified: 4
New onset or recurrence of lymphoproliferative disorder/ Pseudolymphoma/ Lymphomatous drug eruption	5 (0.08%)	1 Pfizer (Brumfiel <i>et al.</i> <sup>37</sup> ), 1 Pfizer (Mintoff <i>et al.</i> <sup>150</sup> ), 2 Astrazeneca (Panou <i>et al.</i> <sup>170</sup> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ).	Pfizer: 2 Astrazeneca: 2 Not Specified: 1
New onset of psoriasis	5 (0.08%)	1 Pfizer (Lehman <i>et al.</i> <sup>97</sup> ), 1 Covishield (Nagrani <i>et al.</i> <sup>106</sup> ), 1 Moderna (Pesqué <i>et al.</i> <sup>154</sup> ), 1 Pfizer (Ricardo <i>et al.</i> <sup>168</sup> ), 1 Pfizer (Song <i>et al.</i> <sup>200</sup> ).	Pfizer: 3 Moderna: 1 Covishield: 1
Cutaneous thrombosis/Skin necrosis	5 (0.08%)	1 Astrazeneca (Ramessur <i>et al.</i> <sup>69</sup> ), 2 Pfizer (Gruenstein <i>et al.</i> <sup>109</sup> ), 1 Astrazeneca (Chen <i>et al.</i> <sup>132</sup> ), 1 Pfizer (Aoki <i>et al.</i> <sup>144</sup> ).	Pfizer: 3 Astrazeneca: 2
Urticarial vasculitis	4 (0.07%)	1 Moderna (Larson <i>et al.</i> <sup>92</sup> ), 1 Not specified (Dash <i>et al.</i> <sup>115</sup> ), 1 Pfizer (Holmes <i>et al.</i> <sup>124</sup> ), 1 Pfizer (Tihy <i>et al.</i> <sup>130</sup> ).	Pfizer: 2 Moderna: 1 Not Specified: 1
Reaction in breastfed infant	4 (0.07%)	1 Moderna (McMahon <i>et al.</i> <sup>138</sup> ), 3 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ).	Pfizer: 3 Moderna: 1
Generalized erythrodermic/ Sub-erythrodermic reaction	4 (0.07%)	1 Moderna (Wei <i>et al.</i> <sup>10</sup> ), 1 Pfizer (Hussain <i>et al.</i> <sup>86</sup> ), 1 Pfizer (Annabi <i>et al.</i> <sup>108</sup> ), 1 Pfizer (Wong <i>et al.</i> <sup>134</sup> ).	Pfizer: 3 Moderna: 1
New onset lichen planus	4 (0.07%)	1 Pfizer (Merhy <i>et al.</i> <sup>78</sup> ), 1 Pfizer (Piccolo <i>et al.</i> <sup>149</sup> ), 1 Not specified (Sharda <i>et al.</i> <sup>166</sup> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ).	Pfizer: 2 Not Specified: 2
Flare of cutaneous lupus erythematosus	4 (0.07%)	1 Pfizer (Niebel <i>et al.</i> <sup>50</sup> ), 1 Astrazeneca (Kreuter <i>et al.</i> <sup>87</sup> ), 1 Moderna (Joseph <i>et al.</i> <sup>131</sup> ), 1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ).	Pfizer: 2 Astrazeneca: 1 Moderna: 1
Stevens Johnson syndrome/ TEN	4 (0.07%)	1 Astrazeneca (Dash <i>et al.</i> <sup>53</sup> ), 1 Moderna (Kong <i>et al.</i> <sup>94</sup> ), 1 Pfizer (Bakir <i>et al.</i> <sup>145</sup> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ).	Pfizer: 1 Astrazeneca: 1 Moderna: 1 Not Specified: 1
Acute generalized exanthematous pustulosis	4 (0.07%)	1 Astrazeneca (Annabi <i>et al.</i> <sup>108</sup> ), 1 Pfizer (Tihy <i>et al.</i> <sup>130</sup> ), 1 Moderna (Agaronov <i>et al.</i> <sup>207</sup> ), 1 Pfizer (Juarez Guerrero <i>et al.</i> <sup>230</sup> ).	Pfizer: 2 Astrazeneca: 1 Moderna: 1
Radiation recall phenomena	3 (0.05%)	2 Pfizer (Soyfer <i>et al.</i> <sup>30</sup> ), 1 Coronavac (Afacan <i>et al.</i> <sup>52</sup> ).	Pfizer: 2 Coronavac: 1
Lichenoid reactions	3 (0.05%)	1 Pfizer (Burlando <i>et al.</i> <sup>11</sup> ), 1 Coronavac (Durmaz <i>et al.</i> <sup>118</sup> ), 1 Pfizer (Onn <i>et al.</i> <sup>198</sup> ).	Pfizer: 2 Coronavac: 1

**Table 1 Continued**

SARS-CoV-2 vaccine-related dermatological manifestations	Number of cases (N = 5941) (100%)	Cases reported by vaccine type* (publication's first author)	Overall reported cases by vaccine type (if available)
Varicella	3 (0.05%)	1 Pfizer (Nanova <i>et al.</i> <sup>43</sup> ), 1 Pfizer (Said <i>et al.</i> <sup>159</sup> ), 1 Moderna (Said <i>et al.</i> <sup>159</sup> ).	Pfizer: 2 Moderna: 1
Generalized pustular psoriasis	3 (0.05%)	1 Coronavac (Onsun <i>et al.</i> <sup>70</sup> ), 1 Astrazeneca (Elamin <i>et al.</i> <sup>119</sup> ), 1 Pfizer (Perna <i>et al.</i> <sup>141</sup> ).	Pfizer: 1 Astrazeneca: 1 Coronavac: 1
Livedo reticularis	3 (0.05%)	3 Pfizer (McMahon <i>et al.</i> <sup>138</sup> ).	Pfizer: 3
Symmetrical drug-related intertriginous and flexural exanthema (Sdrife)	3 (0.05%)	1 Astrazeneca (Lim <i>et al.</i> <sup>116</sup> ), 2 Pfizer (Hai <i>et al.</i> <sup>180</sup> ).	Pfizer: 2 Astrazeneca: 1
Acneiform eruption	3 (0.05%)	3 Coronavac (Rerknimitr <i>et al.</i> <sup>175</sup> ).	Coronavac: 3
Erythema nodosum	3 (0.05%)	1 Covishield (Mehta <i>et al.</i> <sup>151</sup> ), 1 Medigen (Hsu <i>et al.</i> <sup>171</sup> ), 1 Not specified (Grieco <i>et al.</i> <sup>192</sup> ).	Covishield: 1 Medigen: 1 Not Specified: 1
Fascial neutrophilic eruption	2 (0.03%)	2 Moderna (Merril <i>et al.</i> <sup>107</sup> ).	Moderna: 2
Vitiligo	2 (0.03%)	1 Pfizer (Aktas <i>et al.</i> <sup>76</sup> ), 1 Moderna (Kaminetsky <i>et al.</i> <sup>164</sup> ).	Pfizer: 1 Moderna: 1
Annular rash	2 (0.03%)	1 Jj (Song <i>et al.</i> <sup>42</sup> ), 1 Astrazeneca (Kim <i>et al.</i> <sup>224</sup> ).	Astrazeneca: 1 JJ: 1
Henoch-Schonlein purpura	2 (0.03%)	1 Astrazeneca (Naitlho <i>et al.</i> <sup>190</sup> ), 1 Astrazeneca (Sirufo <i>et al.</i> <sup>195</sup> ).	Astrazeneca: 1, 1
Rosacea/Rosacea like	2 (0.03%)	1 Astrazeneca (Ciccarese <i>et al.</i> <sup>123</sup> ), 1 Pfizer (Ciccarese <i>et al.</i> <sup>123</sup> ).	Pfizer: 1 Astrazeneca: 1
Granuloma annulare	2 (0.03%)	2 Not specified (McMahon <i>et al.</i> <sup>138</sup> ).	Not Specified: 2
Generalized dermal hypersensitivity reaction	2 (0.03%)	1 Moderna (Chopra <i>et al.</i> <sup>121</sup> ), 1 Moderna (Myrdal <i>et al.</i> <sup>172</sup> ).	Moderna: 2
Dermatomyositis	1 (0.02%)	1 Pfizer (Niebel <i>et al.</i> <sup>179</sup> ).	Pfizer: 1
Regression of viral wart	1 (0.02%)	1 Astrazeneca (Plaszczynska <i>et al.</i> <sup>174</sup> ).	Astrazeneca: 1
Raynaud phenomenon	1 (0.02%)	1 Astrazeneca (Urban <i>et al.</i> <sup>178</sup> ).	Astrazeneca: 1
Eruptive angiomatosis	1 (0.02%)	1 Pfizer (Zengarini <i>et al.</i> <sup>165</sup> ).	Pfizer: 1
Eosinophilic cellulitis	1 (0.02%)	1 Pfizer (de Montjoye <i>et al.</i> <sup>152</sup> ).	Pfizer: 1
Acantholytic dermatosis	1 (0.02%)	1 Moderna (Tihy <i>et al.</i> <sup>130</sup> ).	Moderna: 1
Flagellate purpura	1 (0.02%)	1 Astrazeneca (Heck <i>et al.</i> <sup>120</sup> ).	Astrazeneca: 1
Pigmented purpuric dermatosis	1 (0.02%)	1 Pfizer (Tihy <i>et al.</i> <sup>130</sup> ).	Pfizer: 1
Purpura fulminans	1 (0.02%)	1 Moderna (Griss <i>et al.</i> <sup>161</sup> ).	Moderna: 1
Acute generalized exanthematous pustulosis	1 (0.02%)	1 Astrazeneca (Wu <i>et al.</i> <sup>137</sup> ).	Astrazeneca: 1
Livedo racemosa	1 (0.02%)	1 Pfizer (Annabi <i>et al.</i> <sup>108</sup> ).	Pfizer: 1
Cutaneous mucormycosis	1 (0.02%)	1 Moderna (Shah <i>et al.</i> <sup>72</sup> ).	Moderna: 1
Regression of lymphoproliferative disorder	1 (0.02%)	1 Pfizer (Gambichler <i>et al.</i> <sup>73</sup> ).	Pfizer: 1
Psoriasiform eruption	1 (0.02%)	1 Moderna (Larson <i>et al.</i> <sup>92</sup> ).	Moderna: 1
Lichen striatus	1 (0.02%)	1 Pfizer (Belina <i>et al.</i> <sup>127</sup> ).	Pfizer: 1
Pityriasis lichenoides et varioliformis acuta (Pleva)	1 (0.02%)	1 Pfizer (Sechi <i>et al.</i> <sup>169</sup> ).	Pfizer: 1
Rowell's syndrome	1 (0.02%)	1 Pfizer (Gambichler <i>et al.</i> <sup>6</sup> ).	Pfizer: 1
Acrocyanosis	1 (0.02%)	1 Pfizer (Pileri <i>et al.</i> <sup>23</sup> ).	Pfizer: 1
Prurigo nodularis	1 (0.02%)	1 Pfizer (Tihy <i>et al.</i> <sup>130</sup> ).	Pfizer: 1

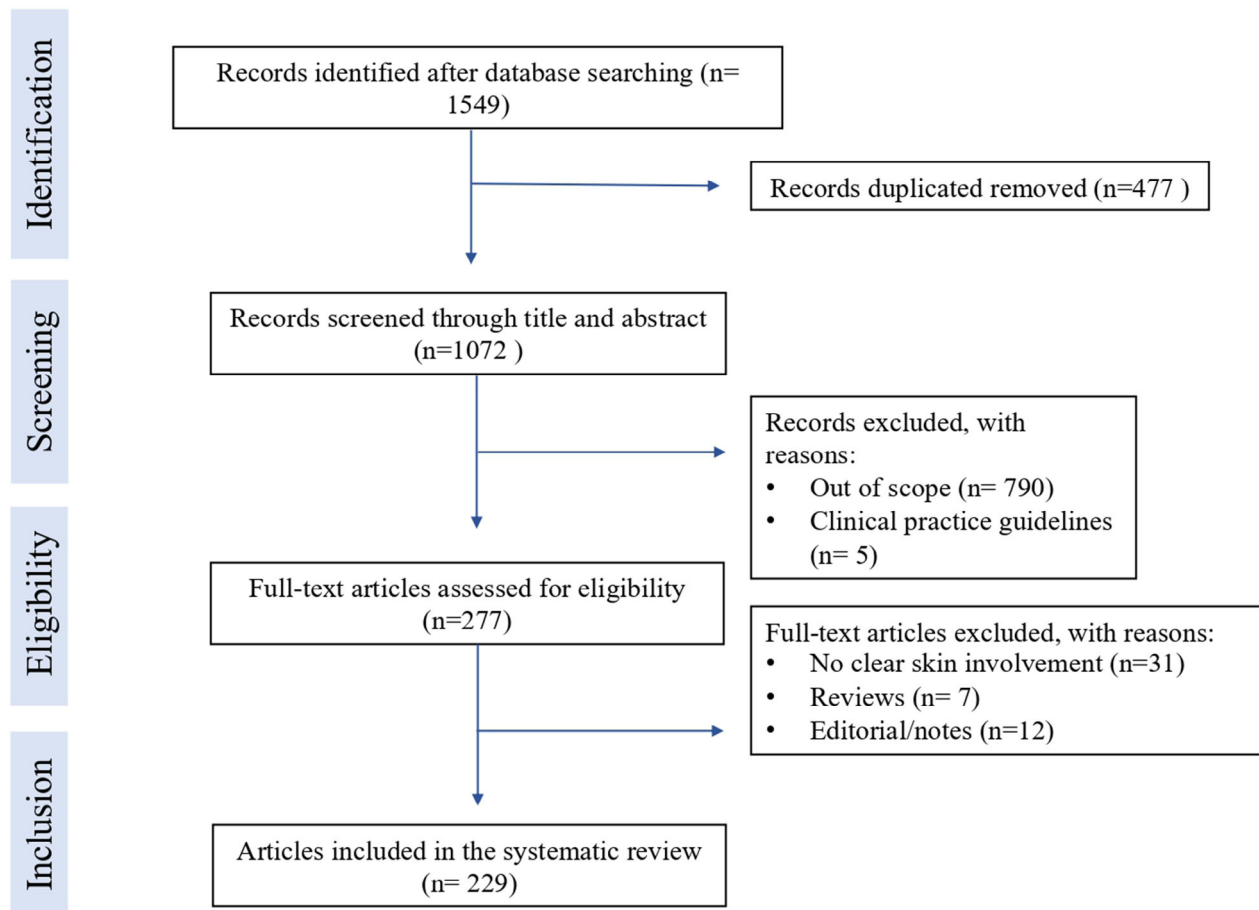
JJ = Johnson & Johnson vaccine.

concerns mRNA vaccine technology, Lopez-Valle *et al.*<sup>17</sup> highlight how an immune-mediated hypersensitivity mechanism seems unlikely because of the lack of previous sensitization to lipid-nanoparticle-mRNA and the presence of low potential hypersensitivity excipients. On the contrary, the authors hypothesized that delayed injection-site reaction could be mediated by

nonspecific inflammation in the spectrum of normal immune response.

### Urticaria

Urticarial rashes are the second most frequent SARS-CoV-2 vaccine-related dermatological manifestations, with a total of 647



**Figure 1** Literature search and article selection

patients reported so far in the extant literature. The largest cohort has been collected in the manuscript of Robinson *et al.*<sup>231</sup> where 376 urticarial rashes following Moderna vaccine ( $n = 321$ ) and Pfizer-BioNTech mRNA ( $n = 55$ ) have been reported. Polyethylene glycol (PEG), often known as macrogol, is a hydrophilic polymer contained in one of the vaccines in Pfizer-BioNTech's excipients (ALC-0315). To date, reactions to PEG in other vaccines have not been reported, insofar as PEG has not been a commonly used excipient in vaccines until now. Currently, it is the only excipient in Pfizer-BioNTech's vaccine with recognized allergenic potential. However, the mechanism of sensitization to PEGs remains unknown. It has not yet been clarified whether PEG should be held accountable for anaphylaxis reactions and urticarial manifestations observed after administration of the vaccine.<sup>236</sup>

### Angioedema

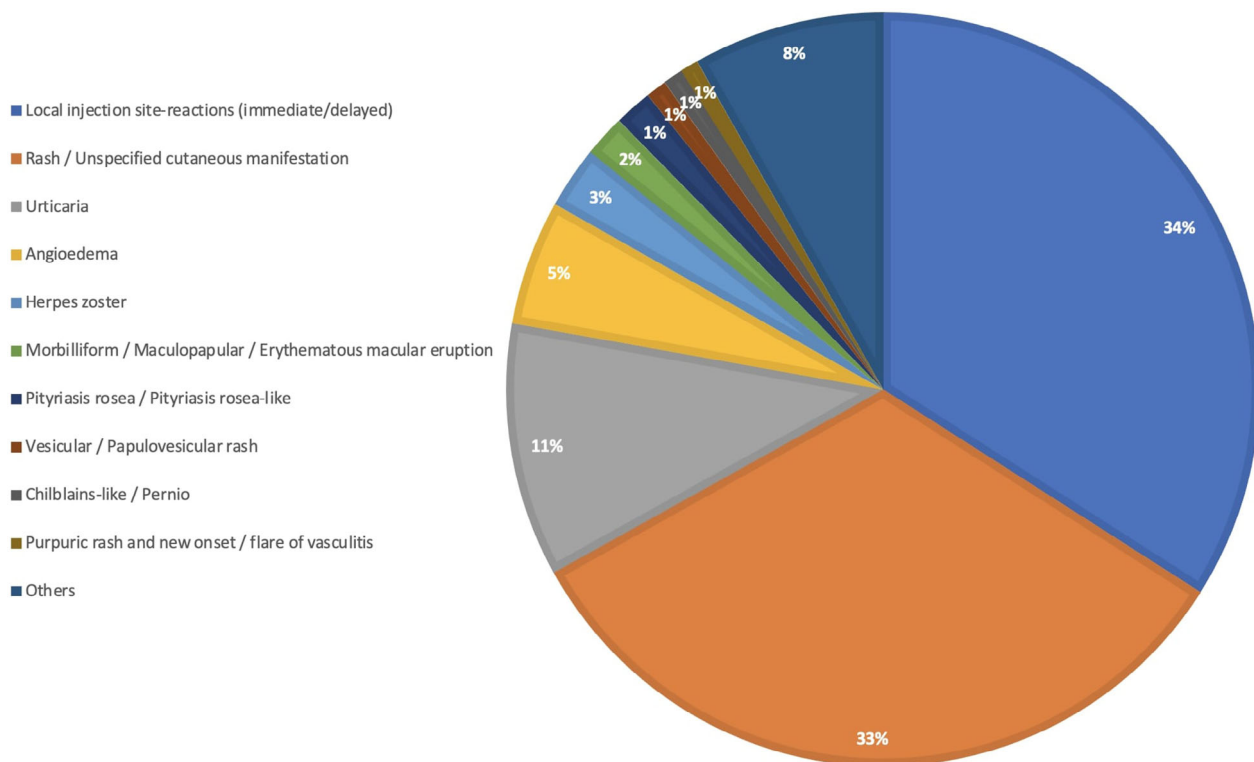
Angioedema accounts for 5.35% of all gathered cutaneous manifestations in this systematic review, with the largest cohort reported by Robinson *et al.*<sup>231</sup> in Moderna-vaccinated health-care workers. Overall, 318 cases were included in our research. Bianchi *et al.*<sup>13</sup> investigated the potential role of skin prick and

intradermal testing to investigate anaphylaxis in patients developing angioedema after Pfizer BioNTech vaccine, with no conclusive results.

### Vasculopathic processes

SARS-CoV-2 vaccine-related vasculopathic processes have been described in different clinical patterns, such as chilblains-like/pernio ( $n = 52$ ), purpuric rash and vasculitis ( $n = 46$ ), and acrocyanosis ( $n = 1$ ). Several histological findings have been described. In Lopez *et al.*<sup>18</sup>, histopathological examination of an asymptomatic violaceous toe discoloration revealed superficial and deep infiltrate of lymphocytes around vessels and eccrine glands, with papillary edema in absence of thrombi or vasculitis. Immunohistochemistry staining for SARS-CoV-2 of the tissue was negative. These findings confirmed the final diagnosis of mRNA SARS-CoV-2 Pfizer-BioNTech vaccine-induced pernio. In Kha *et al.*<sup>19</sup>, the diagnosis of chilblains was confirmed according to histopathological findings, including perivascular lymphocytic infiltrate (majority CD3+) within the superficial-to-deep reticular dermis and papillary dermal edema. Overall, chilblains seem to have a time of onset of approximately 1 week or





**Figure 2** Graphical representation of the 10 most frequent COVID-19 vaccine-related cutaneous manifestations

less since dose administration.<sup>19,27</sup> Several authors hypothesize that these phenomena could represent the cutaneous expression of a strong type I interferon (IFN-I) response elicited by mRNA vaccines.<sup>237,238</sup> Although a complete understanding of the phenomenon is still missing, SARS-CoV-2 vaccine-related immune response - especially INF-driven - could be involved in eliciting these cutaneous entities. As for purpuric rashes following vaccination, several cases have been described as well. A thorough characterization of vasculitis linked to the Sars-CoV-2 vaccine has been provided by Cohen *et al.*<sup>28</sup>, with biopsy-proven flare of leukocytoclastic vasculitis, 2 days after Pfizer-BioNTech vaccine.

### Herpes zoster

One hundred sixty cases of herpes zoster (HZ) after the COVID-19 vaccine have been reported, the majority of which were by McMahon *et al.*<sup>138</sup> ( $n = 24$  after Moderna vaccine,  $n = 22$  after Pfizer-BioNTech,  $n = 11$  after J&J/Janssen vaccine,  $n = 9$  after not specified vaccine), appearing as an uncommon SARS-CoV-2 vaccine-related complication (160/5941, 2.69%).

In our study, reactivation of herpes zoster virus occurred in similar proportions between the two most administered vaccines ( $n = 78$  after Pfizer-BioNTech vaccine,  $n = 56$  after Moderna vaccine) and to a lesser extent in the others ( $n = 7$  after AstraZeneca vaccine,  $n = 5$  after CoronaVac vaccine,  $n = 1$  after

J&J/Janssen vaccine,  $n = 1$  after Covaxin vaccine,  $n = 9$  after not specified COVID-19 vaccine).

The onset of HZ after vaccine administration is not an uncommon finding, and possible explanations have been debated. As previously reported on the pathogenesis of Hepatitis B inactivated vaccine-related side effects,<sup>239</sup> a possible underlying mechanism relies upon vaccine-related immunomodulation accounting for suppression of cellular immunity, a potential cause of the reactivation of herpetic infection. Notably, although mRNA vaccines are innovative since they do not carry the attenuated virus, they may lead as well to dysregulation of the cell-mediated immune system, explaining HZ occurrence in this cohort of patients.<sup>11</sup>

### Pityriasis rosea and pityriasis rosea-like eruptions

Pityriasis rosea (PR) and PR-like eruptions appeared to be relatively infrequent SARS-CoV-2 vaccine-related cutaneous manifestation (96/5941; 1,62%). The largest number of PR-like eruptions ( $n = 26$ ) were reported in a study by McMahon *et al.*<sup>138</sup>

Most commonly, PR and PR-like eruptions followed Pfizer-BioNTech vaccine administration ( $n = 34$ ). A relatively high number of cases have also been associated with the CoronaVac vaccine ( $n = 29$ ), followed by the Moderna vaccine ( $n = 14$ ) and AstraZeneca vaccine ( $n = 8$ ). Eleven cases were also associated with an unspecified COVID-19 vaccine.

Busto-Leis *et al.*<sup>20</sup> reported 26- and 29-year-old men who developed herald patch 24 hours and 7 days after the second dose of the Pfizer-BioNTech vaccine, respectively. Both were negative to nasopharyngeal PCR test to SARS-CoV-2. Subsequent cutaneous manifestations and skin biopsy were compatible with the diagnosis of PR. One out of two patients presented HHV-6 serology ranging from 1:160 to 1:640. The exact pathogenetic mechanism leading to PR after vaccination is unknown. However, a possible reason why PR occurred after the SARS-CoV-2 vaccine is consistent with the elicitation of a specific immune response against an infectious agent triggered by vaccines, which could distract the cell-mediated control on latent herpes virus infections such as HHV-6/7.<sup>240</sup>

Carballido Vazquez *et al.*<sup>22</sup> described a 35-year-old patient with a single, oval erythematous lesion that appeared after the first dose of Pfizer-BioNTech vaccination which evolved into a papulosquamous rash on the trunk and proximal extremities, flaring up after the second dose. In this case, serological evaluation for human herpesvirus reactivation was negative. History of recent vaccination, lesion morphology and distribution, and negativity for herpesvirus serology were all consistent with a PR-like eruption, according to the criteria defined by Drago *et al.* to distinguish it from PR.<sup>241</sup>

### Delayed inflammatory reaction to dermal hyaluronic acid filler

Among SARS-CoV-2 vaccine-related dermatological manifestations, COVID-19 vaccination seems to be a trigger of hyaluronic acid filler-associated delayed inflammatory reaction (DIR). A total of 23 patients have been gathered, showing DIR more frequently after the Moderna vaccine ( $n = 16$ ) than the BNT162B2 vaccine ( $n = 6$ ). Another case occurred after the administration of a not-specified COVID-19 vaccine.<sup>192</sup>

McMahon *et al.*<sup>138</sup> reported 14 cases of DIR following the Moderna vaccine and only two after the Pfizer-BioNTech vaccine. Munavalli *et al.*<sup>31</sup> presented a case series of four female patients, reporting no medical history of drug allergies, which developed DIR to facial dermal hyaluronic acid filler 1–10 days following the 1st and 2nd doses of Pfizer-BioNTech or Moderna, respectively. All these DIRs occurred after a hyaluronic acid filler was performed more than 1 year before the vaccination. A therapy with lisinopril 5 mg, up to 10 mg in case of minimal improvement, led to complete resolution. Reasons behind the occurrence of DIRs after the COVID-19 vaccine should be tackled by future studies.

### Discussion

We conducted a comprehensive systematic review on SARS-CoV-2 vaccine-related dermatological manifestations, collecting up to 5941 total cases of adverse reaction following vaccine administration. Therefore, types of cutaneous findings were grouped into different main categories. Additional adverse

reactions were also cited in the extant literature, such as erythromelalgia, skin discoloration, pityriasis rubra pilaris, erythema, contact dermatitis, the reaction in the breastfed infant, albeit less frequently observed. However, the nature of the present study does not allow to draw conclusions regarding causality in the relationship between vaccine administration and reported skin manifestations. According to the available data, the most commonly observed SARS-CoV-2 vaccine-related cutaneous affection is local injection-site reactions, followed by rashes or unspecified cutaneous eruptions, urticaria, angioedema, herpes zoster, morbilliform/maculopapular/erythematous macular eruption, pityriasis rosea/pityriasis rosea-like, vesicular/papulovesicular rashes, chilblains-like/pernio, purpuric rash/vasculitis, flushing, new onset of autoimmune blistering disease and other cutaneous manifestations including flares of psoriasis, flares of pre-existing nonspecified dermatological condition and erythema multiforme/multiforme-like.

The vaccines most frequently reported to be associated with skin reactions are Pfizer-BioNTech and Moderna. This finding might be explained by the fact that these two vaccines received authorization, were produced, and were subsequently distributed at different times worldwide. It is noteworthy that less skin reactions have been reported following the AstraZeneca vaccine compared to those observed with Pfizer-BioNTech and Moderna. However, further studies are necessary to clarify the reasons for this difference and to shed light on the underlying mechanisms involved.

Overall, skin involvement following SARS-CoV-2 vaccine administration showed to be more likely to be experienced by female patients ( $n = 1708$ ) compared to male patients ( $n = 379$ ) (ratio 4.5:1). However in few studies, such as the ones by Kadali *et al.*<sup>34</sup> and Riad *et al.*<sup>233</sup>, patients' gender could not be identified from the data provided, yet the overall self-reporting response by female patients was significantly higher in both studies (i.e. 88.5%<sup>233</sup> and 89.35% respectively<sup>34</sup>). These data seem particularly true for local injection-site reactions, which have been reported more commonly in women. The possibility of sampling bias might also be considered in interpreting our findings since the early vaccine doses were first administered to healthcare workers (HCWs), the majority of which are females. More specifically, women seem to account for 70% of the whole health and social care sector worldwide, according to Boniol *et al.*<sup>242</sup> Coherently, most of the cases included in our review, especially the ones collected from registry-based studies<sup>138</sup>, were HCWs. To avoid overstatement of adverse reactions in female patients, with the advance of vaccination campaigns among non-HCWs, future studies should keep track of the frequency of skin-related manifestations in more gender-balanced samples. Additionally, heterogeneity of health care systems in reporting vaccine-related adverse reactions as well as different vaccine distribution worldwide scenarios could partially account for our findings.

Some limitations of the present study should be noted. First, most of the data on SARS-CoV-2 vaccine-related

dermatological manifestations available so far come from case reports, limiting the ability to estimate incidence rates of these side effects. With the advance of vaccination programs worldwide, this does not preclude future studies from focusing on larger samples and populations. Second, although the majority of the patients reported in registry-based studies were healthcare professionals, data on skin manifestations following vaccine administration were self-reported, possibly undermining clinical data collection quality. Third, patients' underlying conditions, except for dermatological diseases, were often not explicitly reported by the authors and consequently were not considered in the analysis of our manuscript. Moreover, causality between vaccine administration and cutaneous eruptions was not always assessed by the authors; hopefully further studies will elucidate the immunological underlying mechanisms responsible for SARS-CoV-2 vaccine-related cutaneous reactions.

## Conclusions

With the introduction of large-scale vaccination programs, patients should be monitored for cutaneous manifestations following vaccine administration, and dermatological evaluation should be offered, when needed. However, if compared to the high number of vaccine doses already administered worldwide, cutaneous adverse reactions seem to be rather infrequent and definitely not life-threatening/severe, albeit heterogeneous and worth being studied. Being largely based on case reports and case series to date, our knowledge of SARS-CoV-2 vaccine-related dermatological manifestations should be further developed, and the underlying mechanisms should be clarified. This will also allow dermatologists to promptly recognize and differentiate vaccine-induced cutaneous manifestations from other clinical entities. With that being said, the COVID-19 challenge for dermatologists is far from over.

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