Cutaneous Reactions Reported after Moderna and Pfizer COVID-19 Vaccination: A Registry-Based Study of 414 Cases

Devon E. McMahon, BA, Erin Amerson, MD, Misha Rosenbach, MD, Jules B. Lipoff, MD, Danna Moustafa, BS, Anisha Tyagi, BA, Seemal R. Desai, MD, Lars E. French, MD, Henry W. Lim, MD, Bruce H. Thiers, MD, George J. Hruza, MD MBA, Kimberly Blumenthal, MD MSc, Lindy P. Fox, MD, Esther E. Freeman, MD PhD



DOI: https://doi.org/10.1016/j.jaad.2021.03.092

Reference: YMJD 15862

To appear in: Journal of the American Academy of Dermatology

Received Date: 23 February 2021

Revised Date: 16 March 2021

Accepted Date: 26 March 2021

Please cite this article as: McMahon DE, Amerson E, Rosenbach M, Lipoff JB, Moustafa D, Tyagi A, Desai SR, French LE, Lim HW, Thiers BH, Hruza GJ, Blumenthal K, Fox LP, Freeman EE, Cutaneous Reactions Reported after Moderna and Pfizer COVID-19 Vaccination: A Registry-Based Study of 414 Cases, *Journal of the American Academy of Dermatology* (2021), doi: https://doi.org/10.1016/j.jaad.2021.03.092.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2021 by the American Academy of Dermatology, Inc.



	D		
lourna	Pre-	nro	ot.
JUUIIU		$\mathbf{p}_{\mathbf{I}}\mathbf{O}$	UL.

- Cutaneous Reactions Reported after Moderna and Pfizer COVID-19 Vaccination: A Registry-Based Study 1 2 of 414 Cases 3 4 Authors: Devon E. McMahon BA,<sup>1</sup> Erin Amerson MD,<sup>2</sup> Misha Rosenbach MD,<sup>3</sup> Jules B. Lipoff MD,<sup>3</sup> Danna Moustafa BS,<sup>1</sup> Anisha Tyagi BA,<sup>1</sup> Seemal R. Desai MD,<sup>4</sup> Lars E. French MD,<sup>5,6</sup> Henry W. Lim MD,<sup>7</sup> Bruce H. 5 Thiers MD,<sup>8</sup> George J. Hruza MD MBA,<sup>9</sup> Kimberly Blumenthal MD MSc,<sup>1</sup> Lindy P. Fox MD,<sup>2</sup> Esther E. Freeman 6 MD PhD<sup>1,10</sup> 7 8 <sup>1</sup>Massachusetts General Hospital, Harvard Medical School, Boston, MA; <sup>2</sup>Department of Dermatology, University of California San Francisco, San Francisco, CA; <sup>3</sup>Department of Dermatology, University of Pennsylvania, 9 Philadelphia, PA; <sup>4</sup>The University of Texas Southwestern Medical Center, Dallas, Texas, Innovative Dermatology, 10 Plano, Texas; <sup>5</sup>Department of Dermatology, University Hospital, Munich University of Ludwig Maximilian, Munich, 11 12 Germany; <sup>6</sup>Dr. Philip Frost, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL; <sup>7</sup>Department of Dermatology, Henry Ford Health System, Detroit, MI, USA; <sup>8</sup>Department 13 14 of Dermatology and Dermatologic Surgery, Medical University of SC, Charleston, SC <sup>9</sup>Department of 15 Dermatology, St. Louis University, St. Louis, MO; <sup>10</sup>Medical Practice Evaluation Center, Mongan Institute, 16 Massachusetts General Hospital, Boston, MA 17 18 **Corresponding Author:** 19 Esther Freeman, MD, PhD 20 Massachusetts General Hospital 21 55 Fruit St, Boston, MA 02114 22 Email: efreeman@mgh.harvard.edu 23 Category: Original Article 24 Manuscript word Count: 2500 25 Tables/Figures: 2 Tables; 3 Figures; 1 Supplemental Appendix (available at 26 https://data.mendeley.com/datasets/3t4zn67nc4/1) 27 Keywords: COVID-19; SARS-CoV-2; dermatology; public health; registry; vaccine; mRNA; Pfizer; Moderna 28 Funding: International League of Dermatological Societies provided grant support to Massachusetts General 29 Hospital for administration and maintenance of the Dermatology COVID-19 registry. The American Academy of 30 Dermatology provided in-kind administrative support. 31 Disclosures: Drs. Freeman, Hruza, Rosenbach, Lipoff and Fox are part of the American Academy of 32 Dermatology (AAD) COVID-19 Ad Hoc Task Force. Dr. French is the President and Dr. Lim is board member of
  - 33 the ILDS. Dr. Thiers is the President of the AAD. Dr. Freeman is an author of COVID-19 dermatology for
  - 34 UpToDate.

- 35 Ethics: The registry was reviewed by the Partners Healthcare (MGH) Institutional Review Board (IRB) and was
- 36 determined to not meet the definition of Human Subjects Research.
- 37

38	Capsu	le Summary
39	•	Across 414 cutaneous reactions to the mRNA COVID-19 vaccines in our registry, the most common
40		morphologies were delayed large local reactions, local injection site reactions, urticaria, and morbilliform
41		eruptions.
42	•	Less than 50% of patients with cutaneous reactions after the first dose experienced second dose
43		recurrence. None reported serious adverse events.
44		
45		
46		
47		
48		
49		
50		
51		
52		
53		
54		
55		
50		
57		
59		
60		
61		
62		
63		
64		
65		
66		
67		

### 68 Abstract

- Background: Cutaneous reactions after mRNA-based COVID-19 vaccines have been reported but are not well
   characterized.
- **Objective**: To evaluate morphology and timing of cutaneous reactions after mRNA COVID-19 vaccines.
- 72 Methods: A provider-facing registry-based study collected cases of cutaneous manifestations after COVID-19
- 73 vaccination.
- **Results**: From December 2020-February 2021, we recorded 414 cutaneous reactions to mRNA COVID-19
- vaccines from Moderna (83%) and Pfizer (17%). Delayed large local reactions were most common, followed by
- 76 local injection site reactions, urticarial eruptions, and morbilliform eruptions. Forty-three percent of patients with
- 77 first dose reactions experienced second dose recurrence.
- 78 Limitations: Registry analysis does not measure incidence. Morphologic misclassification is possible.
- 79 Conclusion: We report a spectrum of cutaneous reactions after COVID-19 mRNA vaccines. Most patients with
- 80 first dose reactions did not develop a second dose reaction, and no patients in the registry developed serious
- 81 adverse events after the first or second dose. These data provide reassurance to patients and providers.

- -

#### 98 Background

In December 2020, the Food and Drug Administration (FDA) issued Emergency Use Authorizations
 (EUAs) for Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273) COVID-19 vaccines.

- 101 Clinical trials for both vaccines reported local injection site reactions and systemic symptoms commonly 102 after both doses.<sup>1, 2</sup> Moderna additionally noted delayed injection site reactions (on/after Day 8) in 244 participants 103 (0.8%) after first dose and in 68 participants (0.2%) after second dose.<sup>1</sup> Moderna's trial also described vesicular,
- 104 urticarial, exfoliative, and maculopapular rashes, as well as facial swelling after cosmetic filler injections.<sup>1</sup>
- However, trials did not fully characterize cutaneous reactions and did not describe whether subjects with reactionsafter the first dose also had reactions with the second.
- 107 Given the importance of widespread vaccination in curbing the pandemic, we aimed to collect cases of 108 cutaneous side effects to the mRNA COVID-19 vaccines to i) describe the morphology and timing of cutaneous 109 reactions to the Pfizer and Moderna vaccines and ii) understand differences in cutaneous reactions between the 110 two vaccine doses to guide vaccine counseling.
- 111

## 112 Methods

Our international registry of cutaneous manifestations of SARS-CoV-2, established in March 2020 as a collaboration between the American Academy of Dermatology and International League of Dermatological Societies, expanded to collect COVID-19 vaccine cutaneous reactions on December 24 2020 shortly after FDA EUAs (www.aad.org/covidregistry).<sup>3</sup> Case entry in the registry was open to healthcare workers only. Collected data were de-identified.

The vaccine registry collected dates for both doses, morphology of cutaneous reaction(s), timing and duration of reaction(s), and treatments. We defined local site reactions as occurring within 3 days of first dose vaccination and delayed large local reactions as 4 or more days after first vaccination. A wheal at the vaccine site was considered an immediate or delayed large local reaction depending on timing.<sup>4</sup> Conversely, we defined urticarial reactions as wheals in a distribution beyond the injection site.

We only included cutaneous reactions reported after vaccination with FDA-approved Pfizer or Moderna mRNA vaccines, which at the time of analysis were being administered mostly to healthcare workers and elderly patients. Both vaccines require two doses 3-4 weeks apart. All respondents who only entered a cutaneous reaction to the first vaccine dose were sent a follow-up email to solicit the presence/absence of a cutaneous reaction to the second vaccine dose. We contacted providers who entered partially completed records to

128 complete all fields. We excluded records where the provider was ultimately unable to provide key variables, e.g.

vaccine brand or which vaccine dose the patient reacted to. We used Stata (Version 16) to descriptively analyze
 data. The Massachusetts General Brigham (MGB) Institutional Review Board exempted this study as not Human

131 Subjects Research.

132

#### 133 Results

From December 24 2020-February 14 2021, 414 unique patients reported one or more cutaneous
reactions to Moderna (83%) or Pfizer (17%) COVID-19 vaccines (Figure 1). Patients were median age 44 (IQR
36-59), 90% female, 78% white, and primarily from the United States (98%) (Table 1). Cases were reported by
dermatologists (30%), other physicians (26%), mid-level practitioners (8.8%), nurses (13%), and other healthcare
workers (22%).

Of 414 records, information about both vaccine doses was available for 180 (43% of cases). Of these, 38/180 (21%) reported reactions after the first dose only, 113/180 (63%) reported a reaction after the second dose only, and 29/180 (16%) reported reactions to both doses (Supplemental Figure 1). Therefore, 29 of 67 patients (43%) of patients who had a cutaneous reaction to the first dose also had a cutaneous reaction to the second dose. Of these 29 patients who reported reactions after both doses, 8 (28%) reported similar reactions to both doses, 8 (28%) reported a lesser reaction to second dose, and 13 (45%) reported a more robust reaction to second dose (Figure 2).

146 There were 343 unique reports of cutaneous manifestations after Moderna vaccination, including 267 147 reported after first dose and 102 reported after second dose. The most common cutaneous reactions were 148 delayed large local reactions (n=175 first; n=31 second dose), local injection site reaction (n=117 first; n=69 149 second), urticaria (n=16 first; n=7 second), morbilliform (n=11 first; 7 second) and erythromelalgia (n=5 first; n=6 150 second) (Table 2). For 215/343 patients (63%), only reactions to the first dose were recorded. Of these, 203 151 (94%) planned to receive the second dose and 12 (5.6%) were not planning to receive the second dose due to 152 concerns regarding their first dose cutaneous reactions. Of those who reported information for both doses 153 (n=130), 28 (22%) reported a reaction to first dose only, 76 (58%) reported a reaction to second dose only, and 26 154 (20%) reported reactions to both doses.

155 There were 71 reports of Pfizer vaccine cutaneous manifestations, including 34 after first dose and 40 156 after second dose. Most common were urticaria (n=8 first; n=6 second dose), local injection site reaction (n=8 157 first; n=8 second), and morbilliform rash (n=6 first; n=3 second). For 21/71 (30%) cases, only reactions to the first

dose were recorded. These included patients who were planning to receive their second dose (n=12) and patients not planning to receive their second dose (n=4) due to concerns regarding their first cutaneous reactions. Of 50 patients with information entered for both Pfizer doses, 10 (20%) reported reactions after the first dose only, 37 (74%) after the second dose only, and 3 (6.0%) had cutaneous reactions after both doses.

162 Of the 414 records, 350 (85%) had timing information. Median time from first vaccination to onset of 163 cutaneous symptoms was 7 days (IQR 2-8), which occurred in two clusters, one between day 1-3 and the other 164 between day 7-8 (Figure 3). The majority of timing data came from patients with reactions on the vaccinated arm 165 only, with local injection site reaction occurring median 1 day (IQR 0-1) and delayed large local reactions 166 occurring median 7 days (IQR 7-8) after vaccination (Supplemental Table 1). Median time from second dose 167 vaccination to cutaneous symptom onset was shorter, occurring at day 1 (IQR 1-2). No urticaria or angioedema 168 reports after the first dose were immediate in onset; all came after one day or more. Of 18 patients who reported 169 urticaria after their first vaccine dose for which information about their second vaccine dose was entered, only 4 170 (22%) developed urticaria after their second dose with most (n=3) reporting more widespread urticaria.

171 Delayed large local arm reactions occurred primarily after Moderna vaccination (94%) median 7 days 172 (IQR 7-8) after first vaccine and lasted median 4 days (IQR 3-6) (Figure 3). The reaction occurred more quickly 173 after the second vaccine dose at median 2 days (IQR 1-3) and lasted median 3 days (IQR 2-5). For patients who 174 had delayed large local reactions after both doses (n=11), 3 (27%) had a larger reaction with the second dose. A 175 smaller group of patients who did not develop any cutaneous reaction after the first vaccine dose developed 176 delayed large local reaction to the second (n=23), which occurred a median of 2 days (IQR 1-3) after second 177 vaccination. 116/207 (56%) of patients with delayed large local reactions also had local site injection reactions. 178 Less common reports of other cutaneous findings with both vaccines included 9 reports of swelling at the 179 site of cosmetic fillers, 8 pernio/chilblains, 10 varicella zoster, 4 herpes simplex flares, 4 pityriasis rosea-like 180 reactions and 4 rashes in infants of vaccinated breastfeeding mothers.

181

# 182 Discussion

183 In this registry-based study, we characterized the morphology and timing of cutaneous reactions for the 184 novel Moderna and Pfizer mRNA COVID-19 vaccines. We observed a broad spectrum of reported reactions after 185 vaccination, from local injection site reactions and delayed large local reactions, to urticaria and morbilliform 186 eruptions, to more unusual reactions such as erythromelalgia, pernio/chilblains, filler reactions, and pityriasis-187 rosea-like eruptions. Among 67 patients with cutaneous findings after the first dose and where information on both

doses was available, only 29 (43%) developed cutaneous symptoms after the second dose. This analysis should
 provide reassurance to healthcare providers counseling patients who had a cutaneous reaction after first dose of
 Moderna or Pfizer vaccine regarding their second dose, as there were no cases of anaphylaxis or other serious
 adverse events.<sup>5</sup>

192 The most commonly reported cutaneous finding after vaccine administration was delayed large local 193 reaction, median 7 days after the first vaccine dose, primarily after Moderna (95%). Second dose delayed 194 reactions generally occurred more quickly (Day 2), and were generally lesser. Similarly, the Moderna clinical trial 195 described 0.8% participants who developed delayed large local reactions after day 8 from the first dose and only 196 0.2% of participants with the second dose, but did not link the reactions from one dose to another, and thus would have missed detecting if patients reacted more quickly to the second dose.<sup>1,6</sup> Rarely, delayed-type 197 198 hypersensitivity reactions have been described after vaccination with symptoms such as large localized swelling, 199 skin nodules and/or induration. These reactions, thought to be T-cell-meditated, have been attributed to 200 ingredients such as neomycin or thimersol and have not been considered a contraindication to subsequent 201 vaccination.<sup>4</sup> Although the etiology of these Moderna delayed large local reactions is unclear, a delayed type 202 hypersensitivity reaction to the excipient polyethylene glycol is one potential etiology.<sup>6</sup>

203 In our registry, there were no severe sequelae identified after the second dose in patients experiencing a 204 delayed large reaction after the first dose. Patients responded well to topical corticosteroids, oral antihistamines, 205 and/or pain-relieving medications. These reactions resolved after a median of 3-4 days. Antibiotics were not 206 required for resolution but were sometimes given by providers concerned that the reaction might be cellulitis, as reported elsewhere.<sup>7</sup> Taken together, these data provide reassurance to clinicians tasked with counseling patients 207 208 who experience a delayed cutaneous arm reaction after their first Moderna dose that i) patients tolerated the 209 second dose without developing severe adverse or allergic events, ii) the rash may recur the second time but is, 210 on average, likely to be less severe and may develop faster, and iii) symptomatic therapies (e.g. ice/pain-211 relief/antihistamines/topical corticosteroids) can be used for treatment without antibiotics.

We additionally observed reactions to Moderna and Pfizer vaccines that had been noted after SARS-CoV-2 infection itself, including pernio/chilblains (e.g., "COVID toes"), erythromelalgia, and pityriasis-rosea-like exanthems.<sup>3, 8, 9</sup> That these exanthems mimic dermatologic manifestations of COVID-19 potentially suggests that a) the host immune response to the virus is being replicated by the vaccine and b) some components of these dermatologic manifestations of the virus are likely to be from immune response to the virus rather than direct viral

effects.<sup>10, 11</sup> Erythromelalgia and pityriasis rosea have been noted in response to other vaccines such as those for
influenza and hepatitis B, although uncommonly.<sup>12-14</sup>

We additionally identified rare patients with facial swelling after both Moderna and Pfizer vaccines associated with prior use of injectable cosmetic filler. This phenomenon was similarly described in 3 subjects in Moderna trial reporting; Pfizer did not report any cases.<sup>1</sup> These reactions may represent delayed hypersensitivity to filler following introduction of an immunologic trigger,<sup>15</sup> and have been previously noted after other viral illnesses<sup>16</sup> and influenza vaccines.<sup>1, 17</sup>

224 It is important to distinguish immediate hypersensitivity reactions, defined by the CDC as including 225 pruritus, urticaria, flushing, angioedema occurring within the first four hours of an injection, from similar reactions that occur >4 hours after injection.<sup>18</sup> This distinction is particularly relevant for urticaria and angioedema, which 226 227 are potential contraindications for a second vaccine dose.<sup>18</sup> Although this registry captured time between 228 vaccination and skin reaction in days rather than hours, none of the first dose urticaria reports or angioedema 229 reports occurred on the day of vaccination, and therefore would not be classified as immediate hypersensitivity. 230 Of the 18 urticaria reports where information was available for both vaccine doses, only 4 had urticaria with their 231 second dose, and none reported anaphylaxis, which should provide reassurance regarding patients who develop 232 urticaria >4 hours after vaccination. Importantly, allergic cutaneous symptoms reported in this study, such as 233 urticaria, angioedema, and/or morbilliform eruptions, may not be caused by allergy to the vaccine but instead 234 related to host immune response or an immunologic reaction to nonsteroidal anti-inflammatory agents commonly 235 taken for pain and fever after vaccination.

236 Another limitation of this registry analysis includes incomplete record follow-up. Since providers only enter 237 data at one point in time, patients have differential lengths of follow-up. To overcome this, we reached out via 238 email to all providers after such patients received second doses; nevertheless, we still mostly report information 239 regarding first vaccine dose reactions. Reporting on the second vaccine dose may be more common when there 240 are symptoms (rather than no reaction) to report. As such, this reporting bias might result in our study 241 demonstrating a "worst case scenario" for the second dose. Still, less than half of patients had recurrence with the 242 second dose. An additional limitation is that the morphology description of vaccine reactions is provider-243 dependent. Future studies are needed to classify morphologies with objectively classifiable clinical images and 244 histopathologic evaluation.

245 We are unable to measure incidence of cutaneous reactions to COVID-19 vaccination through a registry-246 based study, which lacks a denominator. There may be confirmation bias, as providers were more likely to enter

cases with severe or rare manifestations. The registry noted 343 reactions from the Moderna vaccine and only 71
from the Pfizer vaccine, but it will require further population level data to understand if this is a true difference or
related to reporting bias. As of February 22 2021, 53% of allocated vaccine doses in the United States were
Moderna and 47% Pfizer.<sup>19, 20</sup>

251 Ninety percent of vaccine reactions were reported in female patients. It is difficult to assess if there is a 252 true sex difference in likelihood of developing a cutaneous reaction, or whether it might reflect reporting bias, or stem from the healthcare workforce being 76% female.<sup>21</sup> Further, vaccine reactions in this registry were primarily 253 254 in white (78%) patients, which highlights important concerns about disparities in vaccine access, healthcare 255 access after experiencing a potential side effect, differential likelihood of reporting to the registry, and/or recognition of skin reactions by healthcare providers in patients with skin of color.<sup>22, 23</sup> Patients were primarily 256 257 located in the United States (97%); at this time, there were no reports in the registry of cutaneous reactions from 258 patients in low and middle income countries, raising attention to global inequities in COVID-19 vaccine access.<sup>24</sup> 259 We characterize a spectrum of cutaneous reactions reported with novel mRNA vaccines for COVID-19. 260 Certain dermatologic findings echo prior vaccine hypersensitivity knowledge, while newer findings, such as the 261 delayed large local reactions to the Moderna vaccine and filler reactions may suggest new immunologic 262 mechanisms. Pernio/chilblains post-vaccine may suggest an immunologic connection to infection with SARS-CoV-2.8,9 Overall, our data support that cutaneous reactions to COVID-19 vaccination are generally minor and 263 264 self-limited, and should not discourage vaccination.<sup>1, 2</sup> Presence of a cutaneous reaction to the first vaccine dose,

when it appears >4 hours after injection, is not a contraindication to receiving the second dose of the Pfizer or
 Moderna. No patients with these findings experienced anaphylaxis or another severe adverse event. Healthcare

workers must be aware of these potential vaccine reactions and advise patients accordingly. Counseling patients
about potential benefits to receiving a COVID-19 vaccine is equally, if not more, important.

269

## 270 Acknowledgements

271 We would like to acknowledge the following individuals for providing clinical photographs: Latasha Jackson,

272 Audrey Fetch, Stephanie Cebreros-Rosales, Su Luo, Josette McMichael, Jaquelyn Saban, Anne Pylkas, and Gina

273 Sevigny. We also thank Grace Chamberlin at Massachusetts General Hospital for her assistance with

administration of the COVID-19 Dermatology Registry. We thank all the healthcare providers worldwide who

entered cases in this registry.

276

277

# 278 References:

279

280 1. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R et al. Efficacy and Safety of the mRNA-1273

- 281 SARS-CoV-2 Vaccine. N Engl J Med 2020.
- 282 2. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S et al. Safety and Efficacy of the
- 283 BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med 2020;383:2603-15.
- 284 3. Freeman EE, McMahon DE, Lipoff JB, Rosenbach M, Kovarik C, Takeshita J et al. Pernio-like skin lesions
- associated with COVID-19: A case series of 318 patients from 8 countries. J Am Acad Dermatol 2020;83:486-92.
- 286 4. Kelso JM, Greenhawt MJ, Li JT, Nicklas RA, Bernstein DI, Blessing-Moore J et al. Adverse reactions to
- vaccines practice parameter 2012 update. J Allergy Clin Immunol 2012;130:25-43.

5. Shimabukuro TT, Cole M, Su JR. Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the

- 289 US-December 14, 2020-January 18, 2021. JAMA 2021.
- 290 6. Banerji A, Wickner PG, Saff R, Stone CA, Jr., Robinson LB, Long AA et al. mRNA Vaccines to Prevent COVID-
- 19 Disease and Reported Allergic Reactions: Current Evidence and Suggested Approach. J Allergy Clin Immunol
   Prost 2020
- 292 Pract 2020.
- 293 7. Blumenthal KG, Freeman EE, Saff RR, Robinson LB, Wolfson AR, Foreman RK et al. Delayed Large Local
- 294 Reactions to mRNA-1273 Vaccine against SARS-CoV-2. N Engl J Med 2021.
- 295 8. Freeman EE, McMahon DE, Lipoff JB, Rosenbach M, Kovarik C, Desai SR et al. The spectrum of COVID-19-
- associated dermatologic manifestations: An international registry of 716 patients from 31 countries. J Am Acad
- 297 Dermatol 2020;83:1118-29.
- 9. Galvan Casas C, Catala A, Carretero Hernandez G, Rodriguez-Jimenez P, Fernandez Nieto D, Rodriguez-Villa
- 299 Lario A et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide
- 300 consensus study in Spain with 375 cases. Br J Dermatol 2020.
- 301 10. Welsh E, Cardenas-de la Garza JA, Cuellar-Barboza A, Franco-Marquez R, Arvizu-Rivera RI. SARS-CoV-2
- 302 Spike Protein Positivity in Pityriasis Rosea-like and Urticaria-like Rashes of COVID-19. Br J Dermatol 2021.
- 303 11. Colmenero I, Santonja C, Alonso-Riano M, Noguera-Morel L, Hernandez-Martin A, Andina D et al. SARS-
- 304 CoV-2 endothelial infection causes COVID-19 chilblains: histopathological, immunohistochemical and
- 305 ultraestructural study of 7 paediatric cases. Br J Dermatol 2020.

- 306 12. Hamada K, Gleason SL, Levi BZ, Hirschfeld S, Appella E, Ozato K. H-2RIIBP, a member of the nuclear
- 307 hormone receptor superfamily that binds to both the regulatory element of major histocompatibility class I genes
- and the estrogen response element. Proc Natl Acad Sci U S A 1989;86:8289-93.
- 309 13. Confino I, Passwell JH, Padeh S. Erythromelalgia following influenza vaccine in a child. Clin Exp Rheumatol
- 310 1997;15:111-3.
- 311 14. Rabaud C, Barbaud A, Trechot P. First case of erythermalgia related to hepatitis B vaccination. J Rheumatol
  312 1999;26:233-4.
- 313 15. Rice SM, Ferree SD, Atanaskova Mesinkovska N, Shadi Kourosh A. The Art of Prevention: COVID-19
- 314 Vaccine Preparedness for the Dermatologist. Int J Womens Dermatol 2021.
- 315 16. Turkmani MG, De Boulle K, Philipp-Dormston WG. Delayed hypersensitivity reaction to hyaluronic acid
- dermal filler following influenza-like illness. Clin Cosmet Investig Dermatol 2019;12:277-83.
- 317 17. Munavalli GG, Guthridge R, Knutsen-Larson S, Brodsky A, Matthew E, Landau M. "COVID-19/SARS-CoV-2
- 318 virus spike protein-related delayed inflammatory reaction to hyaluronic acid dermal fillers: a challenging clinical
- 319 conundrum in diagnosis and treatment". Arch Dermatol Res 2021.
- 320 18. Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United
- 321 States. https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html (accessed February
- 322 15, 2021).
- 323 19. COVID-19 Vaccine Distribution Allocations by Jurisdiction Moderna.
- 324 https://data.cdc.gov/Vaccinations/COVID-19-Vaccine-Distribution-Allocations-by-Juris/b7pe-5nws (accessed
- 325 February 17, 2021).
- 326 20. COVID-19 Vaccine Distribution Allocations by Jurisdiction Pfizer. https://data.cdc.gov/Vaccinations/COVID-
- 327 19-Vaccine-Distribution-Allocations-by-Juris/saz5-9hgg (accessed February 17, 2021).
- 328 21. Your Health Care Is in Women's Hands Census Bureau https://www.census.gov/library/stories/2019/08/your-
- 329 health-care-in-womens-hands.html (accessed February 15.
- 330 22. Demographic Characteristics of People Receiving COVID-19 Vaccinations in the United States.
- 331 https://covid.cdc.gov/covid-data-tracker/ vaccination-demographic (accessed February 17, 2021).
- 332 23. Buster KJ, Stevens EI, Elmets CA. Dermatologic health disparities. Dermatol Clin 2012;30:53-9, viii.
- 24. Baraniuk C. How to vaccinate the world against covid-19. BMJ 2021;372:n211.
- 334
- 335
- 336

# **Table 1:** Characteristics of cutaneous reactions reported after Moderna or Pfizer COVID-19 vaccination

	Moderna Vaccine Unique Reports N(%) (n=343)	Pfizer Vaccine Unique Reports N(%) (n-71)	Total Unique Reports N (%) (n=414)
Reporter Title	(11=3+3)	(1-71)	(11=414)
Dermatologist	96 (28)	30 (42)	126 (30)
Other Physician	79 (23)	29 (41)	108 (26)
Physician Assistant	10 (2.9)	1 (1.4)	11 (2.6)
Nurse Practitioner	24 (6.9)	2 (2.8)	26 (6.2)
Nurse	49 (14)	5 (7.0)	54 (13)
Other medical professional	85 (25)	4 (5.6)	89 (21)
Patient Age (Median, IQR)	45 (36-60)	42 (36-54)	44 (36-59)
Patient Sex (Female) Patient Race/Ethnicity	314 (92)	60 (85)	374 (90)
White	265 (77)	57 (80)	323 (78)
Asian	38 (11)	8 (11)	46 (11)
Black/African American	8 (2.3)	2 (2.8)	10 (2.4)
Hispanic/Latino	27 (7.9)	4 (5.6)	31 (7.5)
Unknown	4 (1.2)	0	4 (1.0)
Patient Country	007 (22)		100 (00)
United States	337 (99)	66 (93)	403 (98)
Canada	2 (0.58)	1 (1.4)	3 (0.7)
Germany	1 (0.3)	1 (1.4)	2 (0.5)
Israel	- 0	1 (1.4)	1 (0.2)
Italy	-	1 (1.4)	1 (0.2)
United Kingdom	-	1 (1.4)	1 (0.2)
Puerto Rico	1 (0.3)	-	1 (0.2)
Guam	1 (0.3)	-	1 (0.2)
Prior SARS-CoV-2 infection			
No	272 (79)	46 (65)	318 (77)
PCR+	7 (2.0)	4 (5.6)	11 (2.7)
Antibody+	2 (0.6)	2 (2.8)	4 (1.0)
Laboratory+ but type unknown	1 (0.3)	0	1 (0.2)
Clinical suspicion only	10 (2.9)	2 (2.8)	12 (2.9)
Unknown	51 (15)	17 (24)	68 (16)
Past Dermatologic History	206 (86)	E2 (7E)	240 (94)
None Atopio dormotitio	296 (86)	53 (75)	349 (84)
Contact dermatitis	12 (3.3)	2 (2.8)	17 (4.1)
Peoriasis	6 (1 7)	2(2.0) 3(4.2)	9 (2 2)
Urticaria	5 (1.5)	2 (2.8)	7 (1.7)
Acne vulgaris	4 (1 2)	2(2.8)	6 (1 4)
Other	10 (2.9)	4 (5 6)	14 (3 4)
Vaccine Allergy History	10 (2:0)	1 (0.0)	11(0.1)
None	316 (92)	64 (90)	380 (92)
Prior local site reaction	11 (3.2)	2(2.8)	13 (3 1)
Drior urtigoria	2 (0 6)	2 (2.0)	$\frac{13}{2} (0.1)$
	∠ (U.0)		∠ (0.5)
Uner	3 (0.9)	1 (1.4)	4 (1.0)
Diknown Past Modical History	12 (3.5)	4 (5.6)	16 (3.9)
None	210 (61)	AG (65)	256 (62)
Hypertension	210 (01) 55 (16)	40 (00) 8 (11)	200 (02) 63 (15)
Obstructive lung disease	18 (5 2)	0 (TT) 2 (2 0)	20 (13)
Marbid abasity	10 (0.2)	∠ (∠.0) 2 (4.2)	20 (4.0) 17 (4.1)
Nicipiu Obesity Diabetes mellitus	14 (4.1) 1 <i>4 (1</i> 4)	ン (4. <i>∠)</i> 1 (1 <i>A</i> )	17 (4.1) 15 (3.6)
Cardiovascular disease	8 (2 3)	- (1.4) 2 (2 8)	10 (0.0)
Rheumatologic disease	6 (1 7)	2 (2.0) 4 (5.6)	10 (2.4)
Maliananov	5 (1.7)	- (0.0) 2 (4 2)	Q (1 0)
Other	0 (1.0) 00 (0.5)	3 (4.2)	o (1.9)
Uther	29 (8.5)	11 (15)	40 (10)
Unknown	18 (5.2)	1 (1.4)	19 (4.6)

- 343 Table 2: Dermatologic findings reported after the Pfizer or Moderna COVID-19 vaccines. Patients who reported
- 344 dermatologic findings after both vaccine doses are counted in both the first dose and second dose columns
- 345 (n=29).

\_

- 346 347 348

Characteristic	Moderna First Dose (n=267) N(%)	Moderna Second Dose (n=102) N(%)	Pfizer First Dose (n=34) N(%)	Pfizer Second Dose (n=40) N(%)
Cutaneous Reactions <sup>†*</sup>				
Delayed large local reaction	175 (66)	31 (30)	5 (15)	7 (18)
Local Injection Site Reaction	143 (54)	71 (70)	8 (24)	10 (25)
Swelling	117 (44)	69 (68)	6 (18)	6 (15)
Erythema	132 (49)	68 (67)	6 (18)	8 (20)
Pain	94 (35)	60 (59)	8 (24)	7 (18)
Urticaria within 24 hours	0 Ó	2 (2.0)	0 Ó	1 (2.5)
Urticaria after 24 hours	13 (4.8)	5 (4.9)	9 (26)	7 (18)
Urticaria unknown timing	3 (1.1)	0	0	0
Morbilliform	11 (4 1)	7 (6 9)	6 (18)	3 (7 5)
Erythromelalgia	5 (1.9)	6 (5.9)	1 (2.9)	2 (5.0)
Flare of existing dermatologic condition**	3 (1.1)	1 (1.0)	8 (24)	3 (7.5)
Vesicular	4 (1.5)	1 (1.0)	3 (8.8)	2 (5.0)
Pernio/chilblains	3 (1.1)	Û	3 (8.8)	2 (5.0)
Zoster (VZV)	5 (1.9)	0	1 (2.9)	4 (10)
Angioedema	5 (1.9)	0	0	1 (2.5)
Pityriasis rosea	1 (0.4)	0	2 (5.9)	1 (2.5)
Erythema multiforme	3 (1.1)	0	0	0
Filler reaction	3 (1.1)	5 (4.9)	0	1 (2.5)
Vasculitis	2 (0.7)	0	1 (2.9)	0
Contact dermatitis	3 (1.1)	1 (1.0)	0	2 (5.0)
Reaction in breastfed infant		1 (1.0)	2 (5.9)	1 (2.5)
Onset of new dermatologic condition***	2 (0.7)	0	0	2 (5.0)
Petechiae	1 (0.4)	2 (2.0)	1 (2.9)	
Systemic Practices in Patients Properting	7 (2.6)	8 (7.8)	2 (5.9)	3 (7.5)
Cutaneous Reactions				
Fatigue	58 (22)	63 (62)	11 (32)	13 (33)
Myalgia	55 (21)	63 (62)	10 (29)	10 (25)
Headache	46 (17)	54 (53)	9 (26)	6 (15)
Fever	18 (6.7)	42 (41)	4 (12)	4 (10)
Arthralgia	16 (6.0)	28 (27)	5 (15)	8 (20)
Nausea	15 (5.6)	28 (27)	4 (12)	3 (7.5)
Chills	14 (5.2)	47 (46)	4 (12)	5 (13)
Lymphagenopathy	13 (4.9)	9 (8.8)	2 (5.9)	3 (7.5)
	9 (3.4)	4 (3.9)	1 (2.9)	U 1 (0 5)
Uther	10 (3.7)	10 (10)	4 (12)	1 (2.5)

<sup>†</sup> Providers were able to check off multiple dermatologic conditions in each patient

A subset of patients reporting vaccine reactions had prior laboratory confirmed SARS-CoV-2 infection, including 11 who were PCR+ and 4 who were antibody+. Cutaneous reactions for these patients included local injection site reactions (n=5), delayed large local reactions (n=3), urticaria (n=2), morbilliform eruption (n=1), pernio/chilblains (n=1), erythromelalgia (n=1), erythema multiforme (n=1), pityriasis rosea (n=1), and reaction in breastfed infant (n=1).

\*\*Includes flare of herpes simplex virus (n=4), atopic dermatitis (n=2), psoriasis (n=2), urticarial vasculitis (n=1), and unspecified eczema (n=2) \*\*\*Includes Raynaud's (n=2), lichen planus (n=1) and unspecified eczema (n=1)

<sup>+</sup>Other cutaneous first dose reactions included full body skin pain/burning (n=2), hypopigmentation (n=2), Sweet's-like fixed urticarial plaque (n=1), pseudovesiculated patches (n=2), and spongiotic dermatitis (n=1). Other cutaneous second dose reactions included canker sore on tongue (n=1), aphthous ulceration on labium (n=1), monomorphic papular eruption (n=2), eczematous pigmented purpura (n=1), spongiotic dermatitis (n=1), and full body skin pain/burning (n=2)

<sup>1</sup> Other systemic reactions included vomiting (n=4 first dose; n=3 second dose), nasal congestion (n=4; n=3), arm tingling/numbness (n=2; n=1), syncope (n=1; n=2), dizziness (n=1; n=2), hot flashes (n=1 first dose only), metallic taste in mouth (n=1 first dose only), and hematuria (n=1 second dose only)

- 368 Figure 1: Timeline representing the time to onset and duration of the top five most common dermatologic findings
- 369 reported after the Moderna and Pfizer COVID-19 vaccines. Circles represent median time to onset of the
- 370 cutaneous reaction and lines represent median duration of the cutaneous reaction. See Supplemental Table 1 for
- 371 detailed information about timing of vaccine reactions.





- ....

- 383 Figure 2: A depiction of the characteristics of the subset of patients who experienced the same dermatologic
- 384 finding after both the first and second COVID-19 vaccine dose. No patient experienced anaphylaxis or another
- 385 severe adverse event after the second COVID-19 vaccine dose.



\*Different patient photos are used for local site injection reaction p
 1 and dose 2.

- 390 Figure 3: Number of days from vaccination (Day 0) until development of cutaneous reaction after COVID-19
- 391 vaccine. Panel A and B show first and second dose dermatologic findings after Moderna (purple) or Pfizer
- 392 (orange) vaccination. Panel C and D are restricted to patients who received Moderna and developed a rash on
- the vaccinated arm showing local symptoms (light blue) and delayed large local symptoms (dark blue). A top
- 394 left, B top right, C bottom left, D bottom right



395

396

397

398