

A Ten-Year Review of Dermal Filler Adverse Events and Vaccination

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Introduction

Following the authorization of two mRNA COVID-19 vaccinations in December 2020, there was increased media attention surrounding reactions to vaccination associated with dermal filler use. Dermal filler adverse events are reported as medical device reports (MDRs) to the United States Food and Drug Administration (FDA). This project seeks to characterize reporting for dermal filler adverse events associated with vaccination over a 10-year period.

Methods

The MAUDE database was accessed to perform a search of all publicly-available MDRs for the “LMH” product code. This query included all reports from 1/1/2011 up to and including 6/30/2021. These reports were searched for whether they included the text “vacc*” or “immuniz*” to represent variations of the words vaccination or immunization, respectively. Reports were excluded based on the Flow Diagram in Figure 1.

A review of literature was performed on November 21, 2021 in Pubmed using the following search strategy:

- ("Dermal Fillers"[Mesh] OR "Artefill" OR "Bellafill" OR "Belotero" OR "dermal filler" OR "dermal tissue reconstructive material" OR "Eleveess" OR "Hydrelle" OR "injectable dermal reconstructive implant" OR "Juvederm" OR "Restylane" OR "Revanesse" OR "skin filler" OR "skin fillers") AND (("Vaccination"[Mesh]) OR "Vaccines"[Mesh] OR vacc* [tw] OR immuniz* [tw])

Results

In total, there were 10,137 MDRs found for the product code LMH from the period of January 1, 2011 until June 30, 2021. Sixty-one of these included search terms related to vaccination or immunization, and were then reviewed in detail. After excluding duplicates, literature, and reports with other known mechanisms, 19 reports were included. Figure 1 shows the flow diagram for inclusion and exclusion of reports for review.

Results

Figure 1. Flow Diagram for Inclusion and Exclusion of MDRs

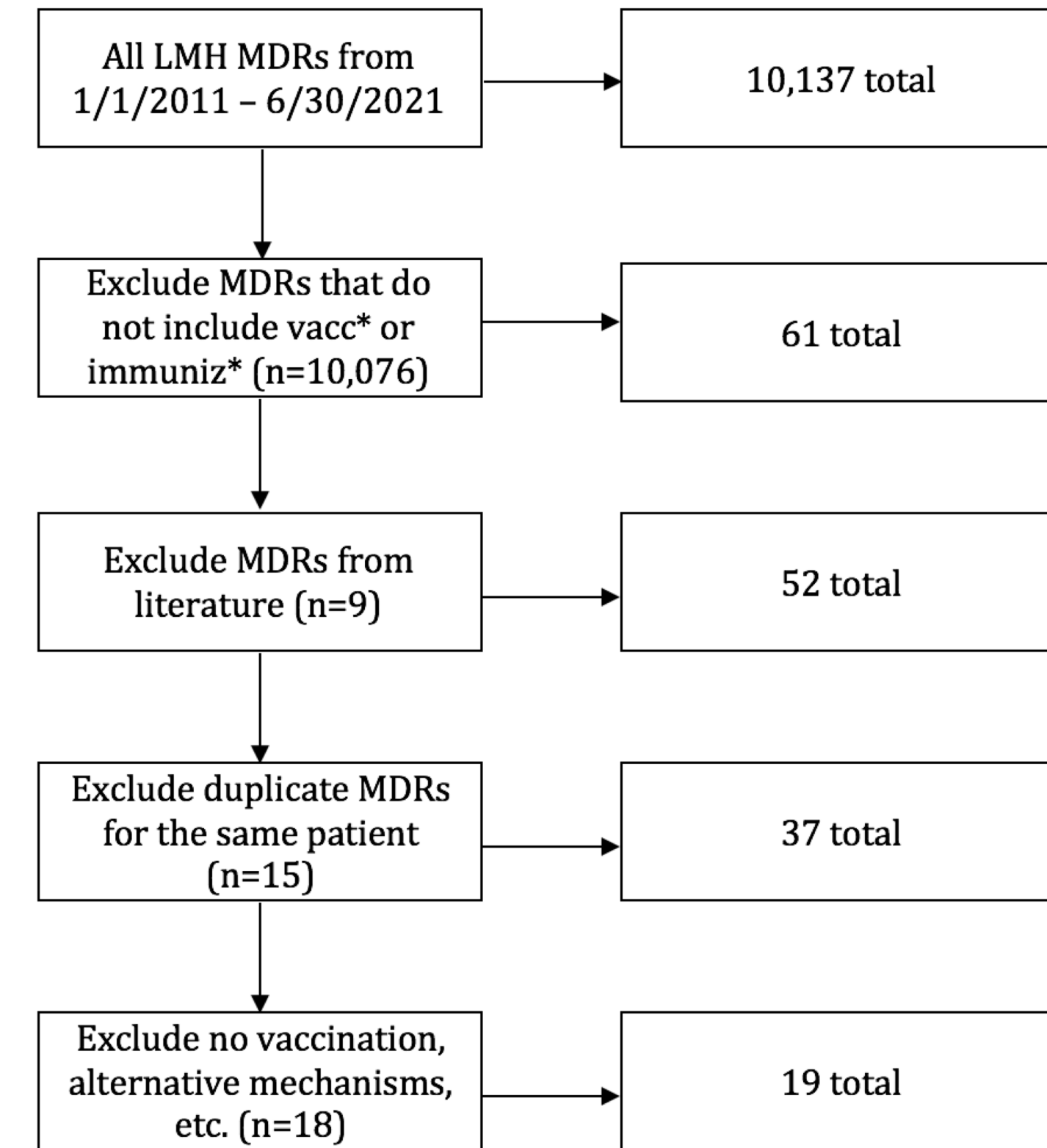


Figure 2. Medical Device Reporting Over Time

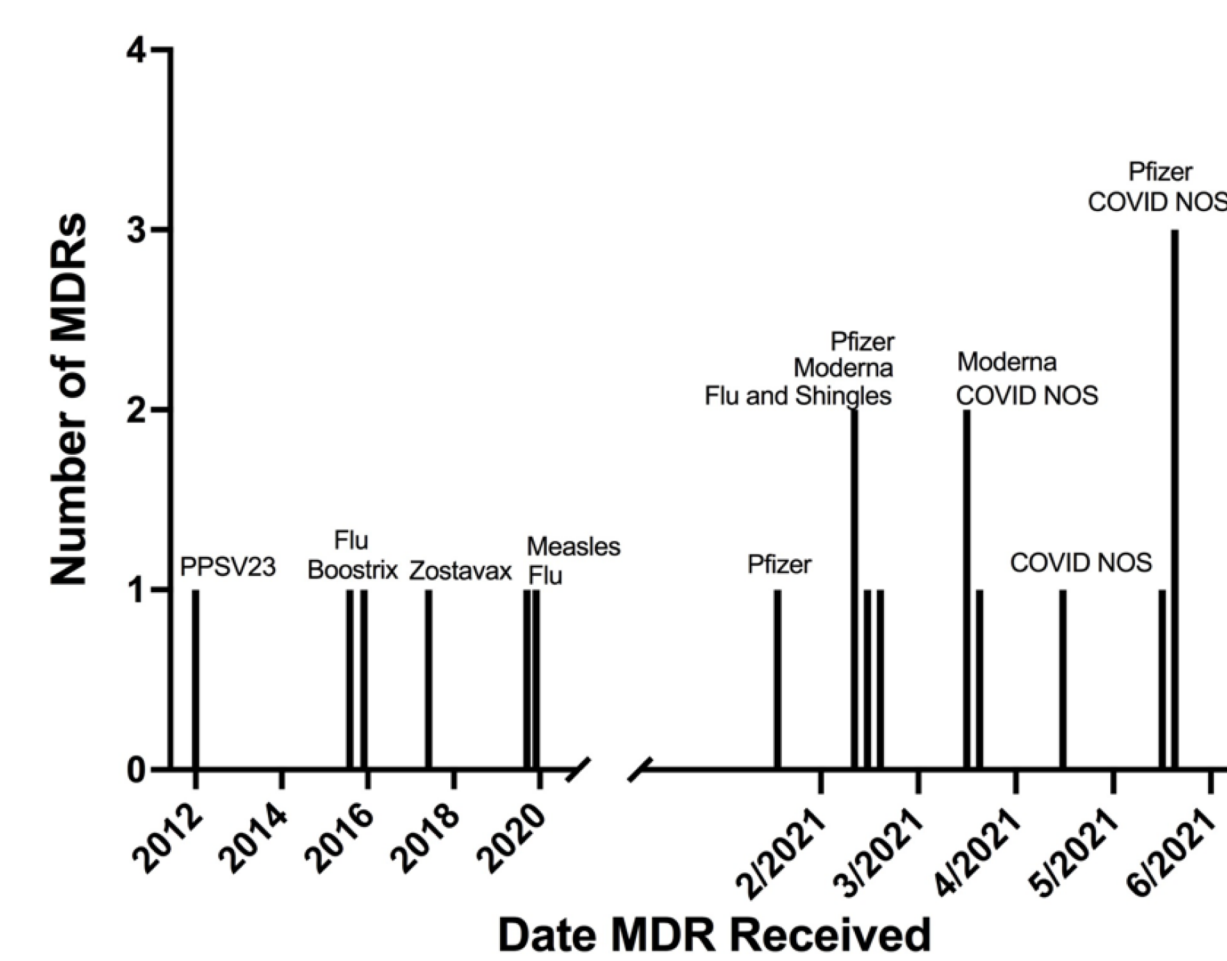


Table 1. Location of Filler Injection and Location of Reaction

Location of Filler*	N*	Location of Reaction	N
Malar Region / Cheeks	8	Same as Filler	13
Lips	7	Different from Filler	3
Perioral / Marionette Lines	6	Same as Filler and Systemic	1
Nasolabial Folds	5	Systemic	1
Tear Troughs / Lower Eyelids	4	Not Specified	1
Glabella	1		
Eyebrow Mounds	1		
Temples	1		
Chin / Mandibular Border	1		
Not Specified	4		

* The total number is greater than 19 as each report may contain more than 1 location

Timing of Reports and Associated Vaccination (Figure 2)

- 6/19 reports were received prior to the pandemic
- 12/19 reports were related to COVID vaccination
- Others included PPSV23, flu, Boostrix (Tdap), Zostavax (shingles), measles

Filler Composition and Location of Injection (Table 1)

- 18/19 were hyaluronic acid, 1 was PLLA
- Most common sites of injection were the malar regions, the lips, the perioral area, nasolabial folds, and tear troughs
- 13/19 reports had a reaction at the same site of filler injection
- 3/19 reports had a different reaction location

Reactions and Timing of Reaction

- 13/19 reports mention swelling
- Other reports reactions include nodules and granuloma (5 reports), redness (5 reports), induration (4 reports) and pain (4 reports)
- 6/19 received vaccination prior to filler
- 10/19 received filler prior to vaccination
- Timing ranged from immediate to over 1 month after filler or vaccination: 7 had reactions in the first day, 4 in the first week, 4 in the first month, 4 unspecified

Results

Management

- Management was often multimodal, but included steroids (13 reports), hyaluronidase (9), antibiotics (9), antihistamines (5), cold compresses (2), and non-steroidal anti-inflammatory medications (2)

Literature Review (Table 2)

Table 2. Review of Literature

Author	Date	Type	Specialty	Vaccine	Filler	Filler Location	Reaction Site	Reaction Timing	Intervention
Rice et al.	1/2021	Review	Dermatology						
Michon et al.	9/2021	Case Report	Dermatology	Pfizer	HA	Tear Trough	Tear Trough	2 days after first dose; 6 months after filler	None
				Pfizer	HA	Zygomatic Arch, Chin, Jawline, Palpebromalar Groove, Tear Trough	Cheeks, Undereye	Several days after first dose; 10 months after filler	Hyaluronidase
Ghasemi et al.	5/2021	Opinion	Other						
Gambichler et al.	10/2021	Review	Dermatology						
Osmond et al.	10/2021	Case Report	Dermatology	Moderna	HA	Chin, Jaw	Chin	1 day after second dose; 3 years after filler	None
Savva et al.	9/2021	Case Report	Other	Pfizer	HA	Lips	Lips	2 days after first dose; 1 month after filler; Second reaction was 2 months after second dose; 4 months after filler	None (first dose); Steroids (second dose)
Buzzaccarini et al.	9/2021	Opinion	Plastic Surgery						
Munavalli et al.	4/2021	Case Report	Dermatology	Pfizer	HA	Temples, Cheeks	Periorbital, Cheeks	2 days after second dose; 2 years after filler	Lisinopril
				Moderna	HA	Lips, Earlobes, Nasolabial Folds, Cheeks	Lip, Earlobe, Zygoma	1 day after second dose; 20 months after filler	Lisinopril
				Moderna	HA	Tear Troughs, Lips	Infraorbital, Perioral, Cheeks	18 hours after first dose; 1 year after filler	Cetirizine (no relief); Lisinopril
				Pfizer	HA	Cheeks	Panfacial, Periorbital	10 days after first dose; >12 months after filler	Lisinopril
Sarigul Guduk et al.	5/2021	Case Report	Other	Rabies, Tetanus	HA	Temple, Lips, Lower Eyelids, Nasolabial Folds	Lips, Temples, Eyelids	3 days after last rabies dose; 6 weeks after filler	Ciprofloxacin, Desloratadine, Steroids (no improvement); Colchicine, Hyaluronidase

Conclusions

- Hyaluronic acid is known to cause a delayed Type IV hypersensitivity reaction, albeit rarely
- This delayed reaction can occur as long as 3 years following implantation
- A distinct immunologic trigger is believed to lead to delayed reactions
- COVID-19 vaccination may be an increasingly common trigger for delayed inflammatory reactions
- Timing of reaction ranged from immediate to over 1 month after vaccination or dermal filler use
- Treatment generally involves hyaluronidase and steroid if necessary
- ACE inhibitors may reduce the risk of delayed hypersensitivity and play a prophylactic role with vaccination
- These findings may affect how patients are counseled prior to filler use, and can also guide provider participation in medical device reporting