

# Melanoma Recurrence after Mohs Micrographic Surgery with MART-1: A Systematic Review and Meta-analysis

Tyler Long, D.O., Natalie Brush, MS, Austin Dunn, MS, Mary Arndt, MS, Eric Parlette, MD



## Background

- **Cutaneous melanoma (CM)** affects about 287,000 new people each year.<sup>1</sup> Worse prognoses are associated with CM located on the head, neck, and trunk compared to extremities.<sup>2</sup> Surgical management continues to be the primary therapeutic approach for CM.<sup>3</sup>
- Current guidelines recommend **wide local excision** of CM but **Mohs micrographic surgery** should be considered for special sites and when there is suspicion of subclinical spread.
- MMS is ideal for the head and neck due to the high recurrence rates of CM due to particular risk features.<sup>4</sup> Unfortunately, **hematoxylin & eosin** frozen sections were notoriously difficult to interpret for CM resulting in poor sensitivity and specificity.<sup>5</sup>

## Objective

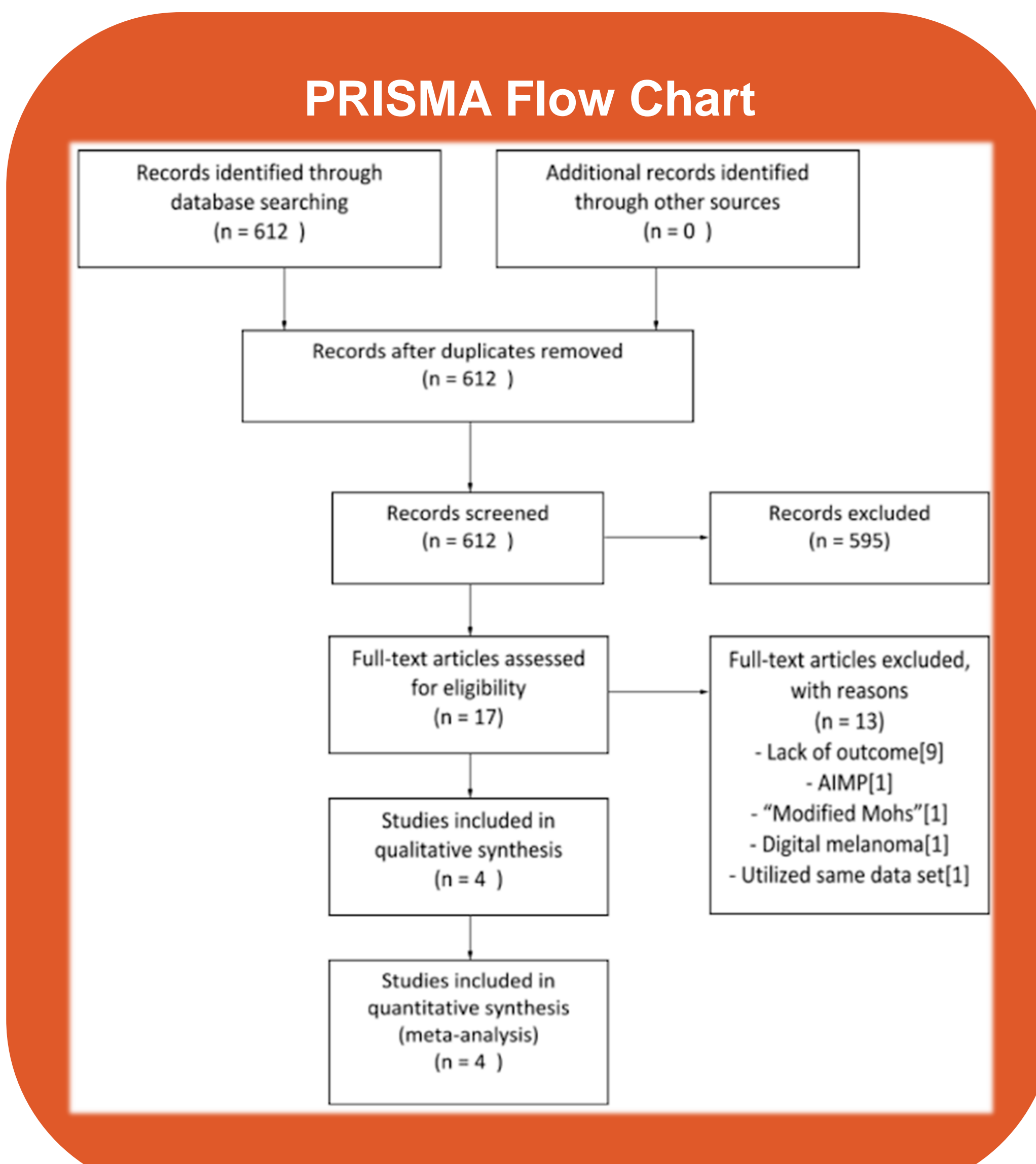
We aim to determine the **rate of local recurrence** of cutaneous melanoma after utilization of Mohs micrographic surgery (**MMS**) with melanocyte-associated antigen recognized by T-cells (**MART-1**) immunohistochemistry (IHS) in frozen sections.

## Methods

The authors followed the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions to execute the study. The authors followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement and checklist

**Search:**  
Pubmed, Medline, and Cochrane databases  
["Mohs" AND "Melanoma"]

**Inclusion:**  
- Utilization of MART-1 immunohistochemistry in frozen sections  
- Melanoma in situ or invasive melanoma  
- Prospective, retrospective, randomized controlled trials  
- Published in a peer-reviewed journal  
- Published in English  
- Full-text



This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

## Results

### Study Characteristics

Study	Foxton <sup>6</sup>	Degeys <sup>7</sup>	Etz Korn <sup>8</sup>	Valentin <sup>9</sup>	p-value
<b>N</b>	62	123	597	2,114	-
<b>Age (mean, range)</b>	63.2 (34-88)	66 (17-94)	66 (18-93)	66 (12-99)	-
<b>Sex</b>					
<b>Female</b>	33 (53.2%)	45 (36.6%)	226 (37.9%)	810 (38.3%)	<0.01
<b>Male</b>	29 (46.8%)	78 (63.4%)	371 (62.1%)	1304 (61.7%)	-
<b>Lesion Type</b>					<b>Total Local Recurrence</b>
<b>Primary</b>	58	117	499	1882	11 0.07
<b>Recurrent</b>	4	6	98	230	4 -
<b>Invasive</b>	8	123	161	200	9 <0.01
<b>Melanoma in-situ</b>	54	0	436	1,914	6 -
<b>Location</b>					<b>Total Local Recurrence</b>
<b>"Other"</b>	7	53	122	990	3 0.10
<b>Head+Neck (Total)</b>	55	70	475	1124	12 -
<b>Face</b>	49	47	355	944	9 -
<b>Neck</b>	3	11	26	82	0 -
<b>Scalp</b>	3	5	45	98	3 -
<b>Ears</b>	NR	7	49	NR	0 -
<b>F/U time, Mean(range)</b>	(3-30 mo)	1273 days	1026 days (4-3167)	3.73 years	
<b>Total Recurrence</b>	0	2 (1.63%)	2 (0.34%)	11 (0.52%)	15 (0.52%)

### Risk of Bias

Study	Risk of bias domains							Overall
	D1	D2	D3	D4	D5	D6	D7	
Degeys(2018)	⊗	⊖	⊕	⊕	⊖	⊕	⊖	⊖
Etz Korn(2015)	⊗	⊕	⊕	⊕	⊕	⊕	⊖	⊖
Foxton(2018)	⊗	?	⊕	⊕	⊕	⊕	⊖	⊖
Valentin(2016)	⊖	⊕	⊕	⊕	⊖	⊕	⊖	⊕

Domains:  
 D1: Bias due to confounding.  
 D2: Bias due to selection of participants.  
 D3: Bias in classification of interventions.  
 D4: Bias due to deviations from intended interventions.  
 D5: Bias due to missing data.  
 D6: Bias in measurement of outcomes.  
 D7: Bias in selection of the reported result.

Judgement:  
 ⊗ Serious  
 ⊕ Moderate  
 ⊖ Low  
 ? No information

## Discussion

- MMS with MART-1 continues to demonstrate lower recurrence rates than conventional excision.<sup>10</sup> Furthermore, the utilization of MART-1 in MMS for CM demonstrated advantages over classical MMS in recurrence<sup>7,11</sup> and surgeon preference.
- Since 2001, the chances of receiving MMS for melanoma has increased 304% in 2016. Only 26.8% of the cases reported use of Immunohistochemistry stains (IHC) - demonstrating a significant increase in utilization over the time period.<sup>12</sup>
- In addition to ease of use/interpretability and outcome improvement, it is important to investigate financial feasibility. Wilson et al. demonstrated that among comprehensive margin assessment techniques for MIS/IM, staged excision using en-face margin assessment (SEEM) and MMS with MART-1 were similar in cost to the healthcare system. The authors noted that SEEM incurred lower costs due to decreased excision code reimbursement and lower number of stages while MMS with MART-1 required less complex reconstruction and the multiple procedure reduction rule. MMS "classic" with H&E generally required more stages, larger margins, and a flap or graft.<sup>13</sup>
- The data presented in this study demonstrates that the increasing utilization of MART-1 in MMS for cutaneous melanoma is warranted and should be recommended, where applicable. The evidence supports current AUC and NCCN recommendations while demonstrating further evidence to expand the use of MMS with MART-1 for CM where local excision continues to demonstrate worse recurrence rates.

## Conclusion

This review demonstrates that MMS with MART-1 IHC in frozen sections has proven to be a technique that produces satisfactory recurrence rates for melanoma in-situ and invasive melanoma. The risk-of-bias of the included studies has been determined to be "moderate" and primarily observational. There appears to be discordance between current guidelines and research supporting broader use of MMS with MART-1.

## References

1. Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer*. 2019;144(8):1941-1953.
2. Balch CM. Cutaneous melanoma: prognosis and treatment results worldwide. *Semin Surg Oncol*. 1992;8(6):400-414.
3. Swetter SM, Tsao H, Bichakjian CK, et al. Guidelines of care for the management of primary cutaneous melanoma. *J Am Acad Dermatol*. 2019;80(1):208-250.
4. Etzkorn JR, Sobanko JF, Shin TM, et al. Correlation Between Appropriate Use Criteria and the Frequency of Subclinical Spread or Reconstruction With a Flap or Graft for Melanomas Treated With Mohs Surgery With Melanoma Antigen Recognized by T Cells 1 Immunostaining. *Dermatol Surg*. 2016;42(4):471-476.
5. Stonecipher MR, Leshin B, Patrick J, White WL. Management of lentigo maligna and lentigo maligna melanoma with paraffin-embedded tangential sections: utility of immunoperoxidase staining and supplemental vertical sections. *J Am Acad Dermatol*. 1993;29(4):589-594.
6. Foxton GC, Elliott TG, Litterick KA. Treating melanoma in situ and lentigo maligna with Mohs micrographic surgery in Australia. *Australas J Dermatol*. 2019;60(1):33-37.
7. Degeys CA, Powell HB, Hsia L-LB, Merritt BG. Outcomes for Invasive Melanomas Treated With Mohs Micrographic Surgery: A Retrospective Cohort Study. *Dermatol Surg*. 2019;45(2):223-228.
8. Etzkorn JR, Sobanko JF, Elenitsas R, et al. Low recurrence rates for in situ and invasive melanomas using Mohs micrographic surgery with melanoma antigen recognized by T cells 1 (MART-1) immunostaining: tissue processing methodology to optimize pathologic staging and margin assessment. *J Am Acad Dermatol*. 2015;72(5):840-850.
9. Valentin-Nogueras SM, Brodland DG, Zitelli JA, González-Sepúlveda L, Nazario CM. Mohs Micrographic Surgery Using MART-1 Immunostain in the Treatment of Invasive Melanoma and Melanoma In Situ. *Dermatol Surg*. 2016;42(6):733-744.
10. Rzepecki AK, Hwang CD, Etzkorn JR, et al. The "Rule of 10s" versus the "Rule of 2s": High complication rates after conventional excision with postoperative margin assessment of specialty site versus trunk and proximal extremity melanomas [published online ahead of print, 2018 Nov 14]. *J Am Acad Dermatol*. 2018;S0190-9622(18)32892-5.
11. Bricca GM, Brodland DG, Ren D, Zitelli JA. Cutaneous head and neck melanoma treated with Mohs micrographic surgery. *J Am Acad Dermatol*. 2005;52(1):92-100.
12. Lee MP, Sobanko JF, Shin TM, et al. Evolution of Excisional Surgery Practices for Melanoma in the United States [published online ahead of print, 2018 Aug 28]. *JAMA Dermatol*. 2019;155(1):124-129.
13. Wilson JG, Geman R, Hamann CR, Vidal NY, LaBoeuf M. Comparison of staged excision and Mohs micrographic surgery with and without MART-1 immunostains for surgical treatment of melanoma of the head, neck, and special sites: A retrospective cohort study. *J Am Acad Dermatol*. 2021;84(1):192-194.

