Clinical and Humanistic Burden of Dermatomyositis and Polymyositis in the US: A Systematic Literature Review

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Background/Objectives

- Dermatomyositis (DM) and polymyositis (PM) are rare heterogenous systemic autoimmune disorders of the skin, muscles and other organs that may have a devastating impact on patients and care partners' lives. A systematic literature review (SLR) was conducted to identify published evidence on disease burden, treatment and unmet needs in DM/PM. The objective of the analysis was to summarize data on the clinical and humanistic burden of DM/PM in the US.

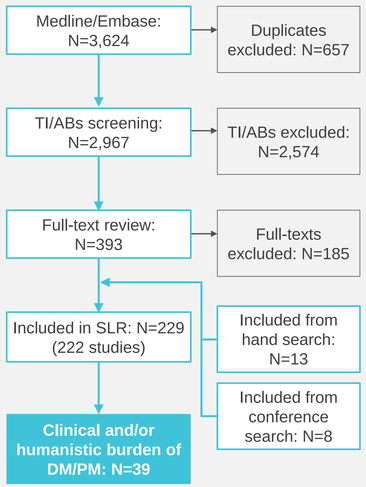
Methods

Study design	Systematic review of literature and qualitative synthesis of evidence
Data Sources	Medline, Embase, references of identified studies, American College of Rheumatology and North American Rheumatic Dermatology Society meeting abstracts (2018-2020)
Eligibility criteria	Primary studies of any design including ≥10 patients with adult- or juvenile-onset DM (JDM)
Relevant outcomes	Clinical burden, humanistic burden, economic burden, disease management and unmet needs
Limitations	Studies in humans, published in English between 2011-2021

Results

- A total of 3,624 records were retrieved from medical databases and 222 studies described in 229 papers were included in data abstraction (Figure 1).
- 39 US studies reported a natural history of disease, comorbidities and/or quality of life (QoL) of DM/PM patients or their caregivers.
- There were 31 (80%) retrospective studies, 4 (10%) prospective longitudinal studies and 4 (10%) cross-sectional surveys, with a sample size ranging from 17 patients to more than 160,000 hospitalizations due to DM/PM.

Figure 1. PRISMA diagram



Results (cont'd)

- **COURSE of JDM**: Between 26–54% of patients with JDM had a chronic disease characterized by persistently active symptoms[1,2]. Ten years post-diagnosis, 36% of JDM patients still had active disease[2].
- **COURSE of DM/PM**: Remission occurred in only 33–38% of adult DM patients.[3,4] Diseases flares were reported by 73% of DM/PM adults within the past year (Figure 2). Their increased frequency trended with longer mean duration of illness and poorer QoL due to increased disability and pain measured by HAQ scores[5] (Figure 3). Prognosis in adult DM patients remained poor with 5-year and 10-year survival estimates of 70%[9] and 56-57%[9,12], respectively. The 10-year survival in DM adults (56.1%) was significantly worse compared to psoriasis (63.1%) (p<0.0001).[12]

Figure 2. Majority of DM/PM adults had disease flare in the past year, reporting muscle weakness as the most common flare symptom[5]

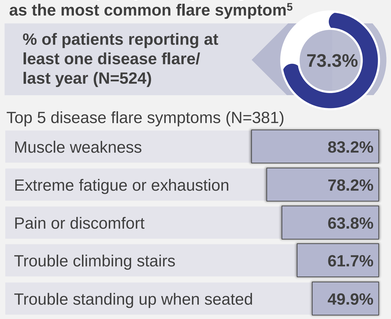
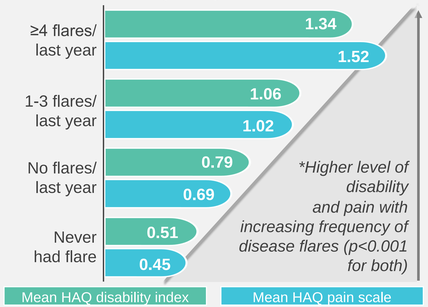


Figure 3. DM/PM adults reported significantly greater disability and pain as frequency of disease flares increased (N=524)[5]



- **COMORBIDITIES**: Adult patients with DM/PM had an increased risk of comorbidities, including infections or serious infections[6-8], malignancies[7,9-13] and cardiovascular disorders (CVDs)[12,14,15], compared to unmatched non-DM/PM controls or patients with psoriasis (Figure 4).

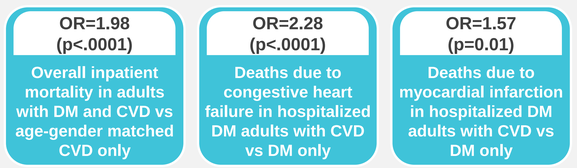
Figure 4. DM/PM adults had significantly increased risk of infections and malignancies compared to controls without DM/PM or patients with psoriasis

Comorbidity	% Patients	DM/PM comparison vs control
Any infection / serious infection	19-42%	↑ **9-16.5%** higher prevalence vs inpatients without DM or without DM/PM (p<0.05)[7,8]
Any malignancy	6-17%	↑ **3.1-3.92%** higher prevalence vs non-DM/PM, inpatients without DM and psoriasis (p<0.05)[7,12,18]
Heart failure / congestive heart failure	1.81-19.8%	↑ **~1%** higher prevalence vs psoriasis (p<0.0001)[12]
Other CVDs*	1.3-5.1%	↓ **2.5-2.8%** lower prevalence vs psoriasis (p<0.05)[12]

* Coronary artery disease, myocardial infarction, cerebrovascular event or transient ischemic attack, peripheral vascular disease.

- Moreover, infections (pneumonia, sepsis) and CVDs were common causes of death in hospitalized DM/PM adults. DM inpatients with comorbid CVD also had significantly increased all-cause mortality than matched non-DM controls with CVD only (Figure 5).

Figure 5. DM inpatients with CVD had significantly higher all-cause and CV-related mortality than inpatients with DM or CVD only[24]



Results (cont'd)

- **QoL**: Adult patients with DM, compared to other dermatologic disorders such as cutaneous T-cell lymphoma (CTCL) and non-melanoma skin cancer/actinic keratoses (NMSC/AK), had a significantly worse Skindex-29 emotional subscore (Table 1)[19], worse SF-36 role-emotional, physical and social functioning subscore[19] and greater fatigue compared to healthy controls (p<0.05)[20]. DM had detrimental impact on QoL measured by Skindex-29 and DLQI which correlated with CDASI skin disease activity.[19]
- **CAREGIVER BURDEN**: JDM affected the entire family with difficulties in family functioning, communication problems, sibling distress and increased number of conflicts[21,22]. Parents of patients with active JDM reported higher levels of worry (p<0.001) and increased difficulty with family relationships (p=0.008) as measured by PedsQL-Family Impact Module, than parents of children with chronic diseases (severe cerebral palsy, birth defects) treated from their home.[21]

Table 1. DM adults had significantly poorer QoL than patients with other chronic diseases and general population

DM / Historic control	Skindex-29 domain*			SF-36^		
	Emot.	Sympt.	Funct.	Physical funct.	Social funct.	Role-emot.
DM	**50.4**	**44.9**	**28.2**	**39.6**	**43.1**	**42.6**
Vulvodynia	50	50	44	*NR*	*NR*	*NR*
CLE	49.1	41.3	28.4	49.6	47.4	47.7
SLE	*NR*	*NR*	*NR*	39.8	37.9	40.1
Epidermolysis	35	49	31	*NR*	*NR*	*NR*
Eczema	41	48	26	*NR*	*NR*	*NR*
Pemphigus	37	37	33	*NR*	*NR*	*NR*
Psoriasis	39	42	23	*NR*	*NR*	*NR*
Acne Vulgaris	41	30	16	*NR*	*NR*	*NR*
CTCL	29	32	22	*NR*	*NR*	*NR*
Rosacea	33	33	16	*NR*	*NR*	*NR*
Alopecia	27	31	14	*NR*	*NR*	*NR*
Vitiligo	35.9	13.9	16.7	*NR*	*NR*	*NR*
NMSC/AK	20	29	9	*NR*	*NR*	*NR*
Depression	*NR*	*NR*	*NR*	45.2	38.5	36.0
Hypertension	*NR*	*NR*	*NR*	46.0	51.4	48.0
CHF	*NR*	*NR*	*NR*	35.1	44.7	43.9
Recent MI	*NR*	*NR*	*NR*	44.4	50.5	47.0
DM2	*NR*	*NR*	*NR*	43.6	49.3	47.6
General. Pop.	*NR*	*NR*	*NR*	50.5	49.9	49.4

* Each scored 0-100 points with higher score indicating poorer QoL; ^ Each scored 0-100 points with lower score indicating poorer QoL. Legend: DM significantly worse; DM significantly better; No difference between DM and control; *NR* = not reported

Conclusions

- **DM/PM are associated with multiple comorbidities such as infections and CVDs that can be serious or life-threatening and result in increased hospitalizations and mortality.**
- **DM/PM affects multiple QoL domains, especially in the physical and social/emotional realm.**
- **Despite various therapies used in clinical practice, a notable proportion of patients seem not to achieve sustainable remission indicating a high residual unmet need.**

References

1. Shah, M., et al. Medicine.2013;92(1):25-41; 2. Patwardhan A, et al. Pediatr Rheumatol Online J. 2012 Sep 20;10(1):34; 3. Wolstencroft P.W., et al. JAMA Dermatology.2018;154(1):44-51; 4. Robinson E.S., et al. Br J Dermatol. 2015;172(1):169-74; 5. Christopher-Stine L., et al. J Manag Care Spec Pharm. 2020;26(11):1424-1433; 6. Prior, D. E., et al. Muscle Nerve.2018;57(6):927-31; 7. Ren Z., et al. Arch Dermatol Res. 2019;311(5):377-87; 8. Murray S.G., et al. Arthritis Care Res. 2015;67(5):673-80; 9. Schiopu, E., et al. Arthritis Res Ther.2012;14(1):R22; 10. Tripathi R., et al. Arch Dermatol Res. 2021;313(6):473-82; 11. Bowerman, K., et al. J Am Acad Dermatol. 2020;83(1):117-22; 12. Narla S. and Silverberg J.I. Arch Dermatol Res. 2020;312(7):507-12; 13. Leatham H., et al. Medicine.2018;97(2); 14. Kim C.H., et al. Journal of Cardiac Failure. 017;23(8):S22; 15. Khojah A., et al. Pediatr Rheumatol. 2019;17; 16. Pachman L.M., et al. Arthritis Rheumatol. 2017;69; 17. Helm M.F., et al. Scand J Rheumatol. 2021;50(3):227-30; 18. Bradford Rice J, et al. J Med Econ. 2016;19(7):649-54; 19. Goreshi R., et al. J AM Acad Dermatol. 2011;65(6): 1107-16; 33; 20. Tarazi, M., et al. Br J Dermatol. 2019;180(6):1468-72; 21. Kountz-Edwards, S., et al. Chronic Illn.2017;13(4):262-74; 22. Ardalan, K., et al. Arthritis Care Res (Hoboken). 2021;73(1):18-29; 23. Robinson A.B., et al. Arthritis Care Res (Hoboken). 2014;66(3):404-10; 24. Linos E., et al. Arthritis Res Ther. 2013;15(1):R7.

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Abbreviations: CDASI, Cutaneous Dermatomyositis Disease Area and Severity Index; CHF, congestive heart failure; CLE, cutaneous lupus erythematosus; CTCL, Cutaneous T=cell lymphoma; CVD, cardiovascular disorder; DLQI, Dermatology Life Quality Index; DM, dermatomyositis; DM2, Type 2 diabetes mellitus; HAQ-DI, Health Assessment Questionnaire – Disability Index; NR, not reported; JDM, juvenile dermatomyositis; NMSC/AK, non-melanoma skin cancer/actinic keratoses; OR, odds ratio; PedsQL, Pediatric Quality of Life Inventory; PM, polymyositis; SF-36, Short Form Health Survey 36; SLR, systematic literature review; TI/Abs, title and abstracts; QoL, quality of life.

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