Myotonic Dystrophy and Cancer Prevalence

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Focus

To identify anatomical sites with elevated cancer prevalence among people with myotonic dystrophy type1 (DM1), type2 (DM2), and myotonic dystrophy not otherwise specified (DM-NOS)

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Muscular Dystrophy Surveillance, Tracking and Research Network (MD STAR*net)*

- Multi-site longitudinal surveillance system
- Identifying and describing individuals with muscular dystrophies
  - Duchenne or Becker Muscular Dystrophy (DBMD)
  - Myotonic Muscular Dystrophy (DM)
  - Limb - Girdle Muscular Dystrophy (LGMD)
  - Facioscapulohumeral Muscular Dystrophy (FSHMD)
  - Emery-Dreifuss Muscular Dystrophy (EDMD)
  - Distal Muscular Dystrophy/Myopathies
  - Congenital Muscular Dystrophy (CMD)
- Sources: medical records (primarily at neuromuscular clinics) and administrative data (such as birth and death certificates)
- Sites: Florida, Iowa, New York, North Carolina, South Carolina, Utah, Virginia

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Collaborators

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Background

- Hospital discharge data & cancer registry data -Sweden and Denmark (Gadalia et al, JAMA 2011)- ↑ risk for **endometrium**, **brain**, **ovary**, and **colon** cancers for all DM combined
- Mayo Clinic retrospective medical record review 1993-2010 (n=307) Type 1 and 2- both types ↑ prevalence for **thyroid**, **Type 1 – melanoma**, **Type 2 –prostate** (Win et al, 2012)
- 20 years of cross-sectional medical record review (n=185 DM1, 67 DM2) (D'Ambrosio et al, Muscle and Nerve, 2023)
  - ↑ risk of **ovarian for DM1**; ↑ risk for **non-melanoma skin, urological, and hematological cancers for DM2**.
- Utah EMR, population-based database and cancer registry (n=281) DM-testicular, endometrial, Non-Hodgkin lymphoma. (Abbott, Johnson, Cannon-Albright, 2016)

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Muscle and Nerve Editorial, April 2023- Cancer in myotonic dystrophy: A new discovery in an old disease (Gadalla and Greene, NIH)

- Seminal epidemiological report of 1658 DM patients (Gadalla et al 2011) showed excess risk for cancers of the brain, endometrium, ovary, and colon, and possibly for thyroid cancer and cutaneous melanoma.
- D'Ambrosio et al. (2023) 20 years of data from EMR compared types of cancers in genetically confirmed DM1 (n = 185), DM2 (n = 67), and selected non-DM neuromuscular controls, found ovarian cancer was more likely in DM1 and hematological or renal/bladder cancers in DM2. (a) Cancer in DM patients versus non-DM controls (5.5% vs 0.7%); (b) no significant association between DM1 repeat size and cancer; and (c) benign tumors affected the same organs known to be at risk for DM-related cancers (skin, thyroid gland, and colon).

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Current recommendations for cancer screening for DM

- The current consensus recommendations for adults with DM1 or DM2 are to follow population-based cancer screening strategies for colon, brain, endometrial, ovarian cancer, largely supported by Mueller (2009) (https://www.myotonic.org/toolkits-publications).
- Consensus-based care recommendations for adults
  - DM1 (Ashizawa 2018); DM2 (Schoser 2019)

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SC-VA MD STARnet Study

- This study broadens the inquiry about prevalence of 20 anatomical sites of cancer among people with DM (n=2054).
- This cross-sectional study can contribute to our understanding of the magnitude of increased prevalence of site-specific cancers documented in clinical records for people with DM1 (n=1311) and DM2 (n=159), and those who have DM-NOS (n=584).

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Methods- Inclusion Criteria

- 2054 individuals who had a health encounter between 2008-2019 and resident sometime during the study years from:
  - Iowa
  - Florida (23 northern counties)
  - New York (21 western counties)
  - North Carolina (33 Piedmont counties)
  - South Carolina
  - Utah
  - Virginia

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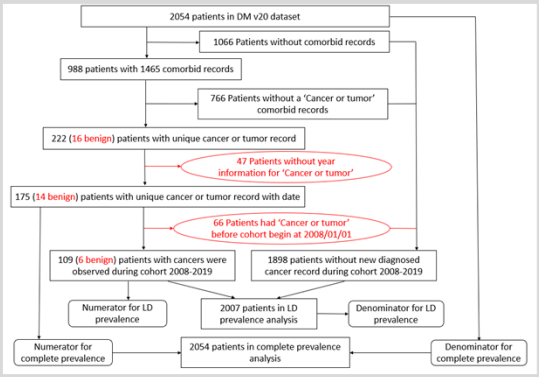

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Statistical Approach

- Expected prevalence (count)=Sum of [Standard prevalence rate in each age- sex-group (from SEER*) x Number of patients in each age- sex- group].
- P-value was calculated from chi-squared test with Yates' correction for small cells:

$$x^2 = \frac{(\text{abs}(\text{Observed count} - \text{Expected count}) - 0.5)^2}{\text{Expected count}}$$

- Used age- and sex-specific US cancer 12 years limited duration standard prevalence in range of 2008-2020 from the SEER 17 registries, age-adjusted to the US Standard Population in 2000 (19 age groups - Census P25-1130). https://www.ncbi.nlm.nih.gov/books/NBK430867/
- Limited-Duration Prevalence represents the proportion of people alive on a certain day who were diagnosed with the disease in the past 12 years. https://surveillance.cancer.gov/prevalence/measures.html#limited To compare to SEER's limited duration prevalence we excluded 47 patients with a 'Cancer or Tumor' comorbid record that were missing the date of diagnosis.
- Standard prevalence rate [SPR]=$\frac{\text{Observed count}}{\text{Expected count}}$.

* Surveillance, Epidemiology and End-Result (SEER) Program

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Individual Characteristics

	Total (N=2054)
Clinical MD Sub Type	
DM NOS	584 (28.4%)
DM1	1311 (63.8%)
DM2	159 (7.7%)
Race/Ethnicity	
Others/Unknown	263 (12.8%)
White	1791 (87.2%)
First Diagnosis of MD	
Mean (SD)	34.9 (19.6)
Median [Min, Max]	36.0 [0, 85.0]
Missing	883 (43.0%)
DNA Test	
No	1064 (51.8%)
Yes	990 (48.2%)
Vital Status until cohort end 12/31/2019	
Deceased	498 (24.2%)
Living	1553 (75.6%)
Unknown	3 (0.1%)

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Individual Characteristics

	Total (N=2054)
Clinical Review Case Status	
Asymptomatic	21 (1.0%)
Definite	1042 (50.7%)
Possible	377 (18.4%)
Probable	614 (29.9%)
State/Site	
FL	196 (9.5%)
IA	413 (20.1%)
NC	271 (13.2%)
NY	408 (19.9%)
SC	296 (14.4%)
UT	370 (18.0%)
VA	100 (4.9%)

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Cancer Prevalence during 12-year study cohort: Type 1 DM compared to the general population

Sites	Age Range	Prevalence (count)	Expected (count)	SPR	P-value
All Sites	58.59 [33, 85]	48	36.13	1.33	0.05
brain/other nervous system	60.5 [51, 70]	2	0.36	5.62	**0.05**
breast	66 [51, 76]	6	8.7	0.69	0.46
colon/rectal	56.4 [43, 85]	5	2.96	1.69	0.37
kidney	61 [44, 78]	2	1.52	1.32	0.99
leukemia	71 [71, 71]	1	0.97	1.03	0.63
melanoma	64.5 [51, 85]	4	2.56	1.56	0.56
oral cavity/pharynx	47.5 [37, 58]	2	0.98	2.04	0.60
ovarian	64 [62, 67]	3	0.51	5.84	**0.01**
pancreatic	49 [49, 49]	1	0.28	3.55	0.68
prostate	63 [58, 68]	2	5.34	0.37	0.22
skin cancer	64 [38, 85]	3	0.17	17.71	**<0.0001**
thyroid	46.57 [33, 68]	7	2.39	2.92	**0.01**

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Cancer Prevalence during 12-year study cohort: Type 2 DM compared to the general population

Sites	Age Range	Prevalence (count)	Expected (count)	SPR	P-value
All Sites	62.61 [36, 84]	17	10.98	1.54	0.08
breast	62.67 [39, 84]	3	2.45	1.23	0.97
colon/rectal	63 [63, 63]	1	0.9	1.11	0.67
leukemia	74 [73, 75]	2	0.26	7.61	**0.02**
liver	36 [36, 36]	1	0.11	9.47	0.22
melanoma	68 [66, 70]	2	0.72	2.77	0.36
non-hodgkin lymphoma	56 [56, 56]	1	0.49	2.06	0.98
oral cavity/pharynx	71 [71, 71]	1	0.29	3.43	0.70
ovarian	70 [70, 70]	1	0.12	8.03	0.29
pancreatic	36 [36, 36]	1	0.09	10.91	0.18
skin cancer	77 [77, 77]	1	0.05	20.13	**0.04**
stomach	54 [54, 54]	1	0.1	9.76	0.21
thyroid	65 [65, 65]	1	0.43	2.31	0.92

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Cancer prevalence during 12-year study cohort: NOS DM compared to the general population

Sites	Age Range	Prevalence (count)	Expected (count)	SPR	P-value
All Sites	57.55 [37, 76]	38	26.08	1.46	**0.02**
brain/other nervous system	67.33 [58, 75]	3	0.17	17.36	**<0.0001**
breast	54.38 [41, 65]	8	5.76	1.39	0.47
colon/rectal	63.33 [59, 71]	3	2.26	1.33	0.87
esophagus	61.5 [60, 63]	2	0.1	19.12	**<0.0001**
leukemia	70 [70, 70]	1	0.65	1.55	0.86
melanoma	55 [52, 58]	2	1.82	1.10	0.81
non-hodgkin lymphoma	76 [76, 76]	1	1.18	0.85	0.77
pancreatic	59 [59, 59]	1	0.21	4.67	0.54
prostate	74 [74, 74]	1	4.87	0.21	0.13
skin cancer	64 [64, 64]	1	0.12	8.36	0.27
stomach	60 [60, 60]	1	0.24	4.17	0.60
thyroid	42.67 [37, 46]	3	1.34	2.24	0.33
uterine	40 [40, 40]	1	1.21	0.83	0.79

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Conclusions

In our study:

- DM1 has increased risk for ovarian, non-melanoma skin, thyroid cancer, and marginal significance for brain/other nervous system SPR 1.5, p=0.055.
- DM2 emerges as having risk for leukemia and non-melanoma skin

Compared to the literature:

- Agreement with D'Ambrosio (2023) on DM1 excess risk for ovarian and thyroid cancer.
- Agreement with D'Ambrosio (2023) on DM2 excess risk for hematological (leukemia) and non-melanoma skin cancer.
- Disagreement with D'Ambrosio study (2023) which suggests DM2 is associated with urological cancer
- Agreement with Gadalla et al (2011) which showed DM pts have excess risk for cancers of the brain, ovary, and thyroid cancer.

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