Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Cancer risk in myotonic dystrophy type 1: an updated systematic review and meta-analysis

John McConville

j.mcconville@qub.ac.uk

Queen's University Belfast https://orcid.org/0000-0002-6788-0642

Lesley Anderson

University of Aberdeen

Charlene McShane

Queen's University Belfast

Grace McMacken

Queen's University Belfast

Keela Patricia McConville

keela.mcconville@belfasttrust.hscni.net

Belfast Health and Social Care Trust

Systematic Review

Keywords: Myotonic dystrophy type 1, DM1, cancer, malignancy, systematic review, meta-analysis, standardised incidence ratio, hazard ratio, risk, trinucleotide repeat

Posted Date: November 10th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11651907/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: The authors declare no competing interests.

Cancer risk in myotonic dystrophy type 1: an updated systematic review and meta-analysis

Keela Patricia McConville[1], Lesley Anderson[2], Charlene McShane[3], Grace McMacken [1,3], John McConville[3,4]

Affiliations

1 **Belfast Health and Social Care Trust**, Belfast, United Kingdom

2 Institute of Applied Health Science, University of Aberdeen & Interdisciplinary Institute, **University of Aberdeen**, Aberdeen, United Kingdom

3 **Queen's University Belfast**, Belfast, United Kingdom

4 **South Eastern Health and Social Care Trust**, Dundonald, United Kingdom

Corresponding author: John McConville

j.mcconville@qub.ac.uk

Abstract

Background

Myotonic dystrophy type 1 (DM1) is an autosomal dominant multisystem disorder caused by expansion of a CTG trinucleotide repeat in the 3' untranslated region of the DMPK gene. Several studies have reported increased cancer incidence in individuals with DM1, but estimates have varied and a previous meta-analysis was limited by studies with small sample sizes. We performed an updated systematic review and meta-analysis to quantify overall and site-specific cancer risk in DM1.

Methods

MEDLINE, Embase and Web of Science were searched from database inception to 6 January 2026. Studies reporting cancer incidence in individuals with DM1 were included. Standardised incidence ratios (SIRs) were pooled using random-effects meta-analysis. Hazard ratios and relative risks reported by studies using alternative comparator populations were summarised descriptively. Heterogeneity was assessed using I^2, Cochran's Q, tau-squared and 95% prediction intervals.

Results

Eleven studies met inclusion criteria. Five studies comprising 7,443 individuals with DM1 contributed data to the primary meta-analysis. The pooled Standardised Incidence Ratio (SIR) for all cancers was 1.74 (95% CI 1.51-2.00; I^2=40.6%). Site-specific analyses demonstrated significant increases in risk for ovarian cancer (SIR 8.08, 95% CI 3.92-16.67), uterine cancer (SIR 7.15, 95% CI 4.72-10.83), brain cancer (SIR 6.68, 95% CI 4.06-11.01), thyroid cancer (SIR 5.45, 95% CI 2.14-13.91), pancreatic cancer (SIR 3.69, 95% CI 2.02-6.75), liver cancer (SIR 2.97, 95% CI 1.89-4.68), lymphoma (SIR 2.20, 95% CI 1.17-4.15), melanoma (SIR 1.92, 95% CI 1.10-3.36) and colorectal cancer (SIR 1.92, 95% CI 1.41-2.60). Breast and lung cancer were not significantly elevated. Heterogeneity was low for most site-specific analyses.

Conclusions

Individuals with DM1 experience a significantly increased incidence of cancer. Cancer risk is not uniformly elevated across tissues, with marked increases observed for selected malignancies and little evidence of excess risk for others. These findings support enhanced awareness of cancer susceptibility in DM1 and suggest that DM1 may provide a useful model for investigating relationships between somatic repeat instability and carcinogenesis.

Keywords: Myotonic dystrophy type 1; DM1; cancer; malignancy; systematic review; meta-analysis; standardised incidence ratio; hazard ratio; risk; trinucleotide repeat.

Background

Myotonic dystrophy type 1 (DM1) is an autosomal dominant, multisystem disorder caused by expansion of a CTG trinucleotide repeat within the 3' untranslated region of the *DMPK* gene (Brook et al. 1992; Mahadevan et al. 1992). Disease manifestations involve multiple organ systems including skeletal muscle, cardiac muscle, smooth muscle, brain and endocrine tissues (Wenninger, Montagnese, and Schoser 2018; Turner and Hilton-Jones 2010). Manifestations are believed to be due to the toxic effects of massively expanded trinucleotide repeat-containing RNA transcripts which are trapped in the nuclei. These sequester transcription factors like MBNL1, resulting in widespread dysregulation of RNA processing and splicing (Ho et al. 2004). A distinctive feature of DM1 is progressive somatic instability of the pathogenic repeat (Morales et al. 2023; Morales et al. 2020), leading to marked tissue-specific mosaicism and substantial variation in average repeat length between cells and tissues.

Interest in malignancy risk in DM1 arose initially from observations of an increased prevalence of pilomatricomas, rare hair follicle tumours that are also encountered in inherited cancer predisposition syndromes (Chiaramonti and Gilgor 1978; Mesa-Álvarez et al. 2019; Ciriacks, Knabel, and Waite 2020; Saponaro et al. 2025). Subsequent population-based studies demonstrated an increased incidence of cancer in individuals with DM1, with Gadalla and colleagues reporting a two-fold increase in overall cancer risk in Swedish and Danish cohorts (Gadalla et al. 2011). Since then, several studies have reported elevated risks for specific malignancies including endometrial, ovarian, thyroid and colorectal cancers, although results have varied between studies and individual analyses have often been limited by small sample

sizes (Emparanza et al. 2018; Maya-González et al. 2024; Seo and Park 2024; Alsaggaf et al. 2025).

An earlier meta-analysis by Emparanza et al. incorporated five studies and demonstrated increased risks for several site-specific malignancies (Emparanza et al. 2018). Since that publication, additional population-based studies have substantially increased the number of individuals with DM1 available for analysis. We therefore performed an updated systematic review and meta-analysis to quantify overall and site-specific cancer risk in DM1 and to better characterise the pattern of malignancy associated with the disease.

Main text

Methods:

A systematic search of Medline, Embase and Web of Science was conducted. The search was conducted from database inception to 6th January 2026 to identify all published research on Cancer risk in patients with Myotonic Dystrophy compared to the general population. The search strategy is included in Supplementary materials (Supplement A). Search results were imported into Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) for study screening and management.

Eligible studies were primary research investigations reporting cancer incidence, or cancer risk in individuals with myotonic dystrophy type 1 (DM1) or type 2 (DM2). Quantitative synthesis was limited to DM1 because insufficient data were available for DM2. Animal studies, meta-analyses, conference proceedings without data, studies without comparator to cancer risk in healthy population and studies not examining cancer risk in myotonic dystrophy patients were excluded. All abstracts were reviewed by the primary reviewer (KMcC) and an additional reviewer. All studies identified for full text review were obtained and reviewed. Any

discrepancies between reviewer decisions were discussed and outcome agreed. The process is summarised in the PRISMA diagram (Figure 1).

Most studies reported cancer risk estimates as standardised incidence ratios (SIRs) compared to the general population. All eligible studies reporting SIRs were included in the quantitative synthesis.

Some studies reported cancer risk estimates as hazard ratios or relative risks compared to a control population. Although pooling of HR and RR estimates was considered, these studies were not synthesised quantitatively. Several reports were derived from potentially overlapping underlying cohorts, particularly within the Scandinavian registry literature. Notably, a substantial proportion of HR/RR cancer outcomes arose from cohorts that overlapped with studies contributing to the SIR synthesis. A separate pooled HR/RR analysis could therefore have created the impression of an independent sensitivity analysis despite reliance on some of the same underlying populations. We therefore elected to present HR/RR estimates descriptively, allowing comparison of direction and magnitude of effect without generating a potentially misleading summary statistic. In the supplement section we have included tables with reported hazard ratios and relative risk alongside the forest plots of the SIR meta-analyses for comparison (Supplementary Figures A-U).

When multiple studies reported SIRs, pooled estimates were calculated using random-effects meta-analysis on the logarithmic scale. Random-effects meta-analyses were performed using restricted maximum likelihood estimation. Statistical heterogeneity was assessed using Cochran's Q, I^2 and tau^2 statistics. Where appropriate, 95% prediction intervals were calculated to estimate the range of effects expected in future populations.

Statistical analyses were conducted in RStudio (Posit Software, Boston, MA, USA) using R (R Foundation for Statistical Computing, Vienna, Austria). Random-effects meta-analyses were

performed using the Metafor package. Forest plots were generated in R and exported as 600 dpi TIFF images for publication.

Risk of bias was assessed using the Newcastle-Ottawa Scale for cohort studies. Individual study assessments are presented in Supplementary Table S1.

Given the rarity of DM1, potential overlap between study populations was specifically assessed (Supplementary Table S2). Overlap was identified between the Scandinavian registry studies of Gadalla et al. and Maya-González et al. Only Gadalla et al. was retained for meta-analysis: it represented the larger cohort, reported SIRs, and formed the basis of subsequent investigations of cancer risk in DM1. Maya-González et al. hazard ratios are reported in the supplementary data: the reader should note the overlap with Gadalla. Cohort overlap was also identified between Alsagaf et al. and Wang et al., as both identified DM1 patients using the UK CPRD database. Neither study contributed to the meta-analysis because both reported hazard ratios rather than SIRs. In addition, Wang et al. examined skin cancers only. To avoid potential patient duplication, the melanoma hazard ratio reported by Wang et al. was retained for narrative synthesis and Alsaggaf et al. was excluded.

Results:

Literature Search and Study Characteristics.

The literature search identified 11 studies suitable for inclusion in the systematic review: Table 1 (Abbott, Johnson, and Cannon-Albright 2016; Alsaggaf et al. 2025; Fernández-Torrón et al. 2016; Gadalla et al. 2011; Hameed et al. 2025; Maya-González et al. 2024; Seo and Park 2024; Wang et al. 2018; Win et al. 2012; Zhang et al. 2025; Mohamed, Pruna, and Kaminsky 2013). Most studies were population-based cohort studies that identified individuals with DM1 through specialist clinic databases or national patient registries and subsequently linked these cohorts

to regional or national cancer registries. Study characteristics, quality assessment and reported effect estimates are summarised in Table 1 and Supplementary Table S3.

Risk of bias.

Individual study assessments are presented in Supplementary Table S1. Most included studies were population-based registry studies with robust ascertainment of both DM1 and cancer outcomes and were therefore considered at low overall risk of bias. However, adjustment for potential confounding factors was limited. Most studies adjusted only for age and sex, with no consideration of socioeconomic status, educational attainment, health behaviours, healthcare access, or disability-related factors. As DM1 is associated with cognitive impairment, educational disadvantage and functional disability, residual confounding cannot be excluded.

Meta-analysis: all cancer.

Five studies comprising 7,443 individuals with DM1 reported standardised incidence ratios (SIRs) for all cancers and were included in the primary meta-analysis. The pooled SIR for all cancers was 1.74 (95% CI 1.51-2.00; I^2=40.6%), indicating a significantly increased incidence of cancer in individuals with DM1 (Figure 2). The corresponding prediction interval was 1.36-2.22.

Meta-analysis: individual sites.

Individual site-specific meta-analyses included between two and five studies depending on cancer type. Meta-analysis of site-specific cancers demonstrated substantial variation in cancer risk across tissues (Figure 3). The highest pooled SIRs were observed for ovarian cancer (Figures 4a: SIR 8.08, 95% CI 3.92-16.67), uterine cancer (Figure 4b: SIR 7.15, 95% CI 4.72-10.83), brain cancer (Figure 4c: SIR 6.68, 95% CI 4.06-11.01) and thyroid cancer (Figures 4d: SIR 5.45, 95% CI 2.14-13.91). Significant elevations were also observed for testicular, pharyngeal,

pancreatic, cervical, liver, lymphoma, melanoma and colon/colorectal cancers (Figure 2, supplementary figures a-z). In contrast, pooled estimates for breast and lung cancer were not significantly elevated (Figure 4e&f: Supplementary Figures A-U). Supplementary Figure S4 summarises sites represented in single studies or with categories that were not incorporated into the numerical synthesis.

Hazard Ratios.

In addition to studies reporting SIRs, five studies reported hazard ratios, and one study reported relative risks. Although these outcomes were not pooled because of differences in study design, comparator populations and effect measures, their findings were broadly consistent with the SIR analyses. Most demonstrated increased overall cancer risk in individuals with DM1 and reported elevated risks for several site-specific malignancies. These results are presented with the corresponding Forest plots in Supplementary Figures A-U.

Heterogeneity.

Heterogeneity was generally low, with I^2=0% for most site-specific analyses (Figure 2, supplementary figures a-z). Substantial heterogeneity was observed for thyroid cancer (I^2=83.4%), prostate cancer (I^2=82.5%) and stomach cancer (I^2=74.5%). Prediction intervals were correspondingly broad for these outcomes.

Individual forest plots for all site-specific SIR meta-analyses together with reported hazard ratios and relative risks from non-pooled studies are provided in the Supplementary Materials (Supplementary Figures A-U).

Overall, the pattern of malignancy was non-uniform, with marked elevations in risk observed for selected cancers while other cancer types demonstrated little or no increase above population expectations.

Conclusions.

In this updated systematic review and meta-analysis, we found a significantly increased overall incidence of cancer in individuals with DM1, with a pooled SIR of 1.74. Several site-specific cancers demonstrated particularly marked elevations in risk, including ovarian, uterine, brain and thyroid cancers. In contrast, other common malignancies such as breast and lung cancer showed little evidence of increased incidence. The pattern of cancer risk was therefore non-uniform, suggesting that susceptibility in DM1 is not adequately explained by a generalised increase in malignancy risk but may instead reflect tissue-specific biological effects.

Cancer is the third most common cause of death in myotonic dystrophy, despite reduced life expectancy due to respiratory and cardiac complications (Mathieu et al. 1999). These findings further support the need for awareness of site-specific cancer risks in DM1.

Our findings are broadly consistent with those of Emparanza et al., while substantially extending the available evidence base through the inclusion of more recent population-based studies (Emparanza et al. 2018). The increased number of patients available for analysis has improved precision for a number of site-specific estimates and allowed a more comprehensive assessment of heterogeneity and prediction intervals. Importantly, several associations reported previously remained robust despite the inclusion of additional cohorts, supporting the reproducibility of the observed pattern of cancer risk.

The association between DM1 and cancer is biologically intriguing because it extends beyond a simple epidemiological observation. DM1 is not simply a Mendelian disorder but also one of the

best characterised human diseases of progressive somatic genetic mosaicism. The pathogenic CTG repeat is highly unstable and continues to expand throughout life, generating marked variation in repeat length among tissues and between cells within the same tissue (Morales et al. 2023). In addition, studies examining DM1-associated tumours have demonstrated further expansion of CTG repeats within neoplastic tissue compared with adjacent non-neoplastic tissue (Bañuls et al. 2004; Kinoshita et al. 1997; Kinoshita et al. 2002).

The marked variation in cancer risk observed between tissues is notable. If increased cancer incidence resulted solely from ascertainment bias, reduced physical activity, healthcare utilisation or other non-specific consequences of chronic illness, a more uniform increase across malignancies might be expected and increased risk should be overserved in other late onset inherited myopathies (Bianchi et al., 2016; D'Ambrosio et al., 2023; D'Ambrosio 2023). Instead, the highest risks were observed in a restricted subset of tissues. While the mechanisms underlying this distribution remain uncertain, it is tempting to speculate that tissue-specific differences in repeat instability, DNA repair, transcriptional activity or RNA toxicity may contribute to the observed pattern.

Limitations

Several limitations should be acknowledged. The number of studies available for some site-specific cancers remained small, resulting in wide confidence intervals. Although overall study quality was high, most studies adjusted only for age and sex, and residual confounding cannot be excluded. In particular, few studies adjusted for socioeconomic status, educational attainment, health behaviours or disability-related factors, all of which may differ between individuals with DM1 and the general population. Potential cohort overlap was identified

between Scandinavian registry studies and addressed through exclusion of overlapping datasets from quantitative synthesis. In addition, not all studies clearly distinguished between DM1 and DM2. This is of particular relevance in Northern European populations, where DM2 may approach the prevalence of DM1. Although the majority of included cases are likely to represent DM1, inclusion of a small proportion of individuals with DM2 cannot be excluded and may have influenced risk estimates. Finally, observational studies are unable to determine whether repeat expansion itself is causally related to carcinogenesis or merely associated with other biological processes that influence cancer risk.

List of abbreviations

CI – Confidence Interval

CPRD – Clinical Practice Research Datalink

CTG – Cytosine-Thymine-Guanine (trinucleotide repeat)

DM1 – Myotonic Dystrophy Type 1

DM2 – Myotonic Dystrophy Type 2

DMPK – Dystrophia Myotonica Protein Kinase

HR – Hazard Ratio

I^2 – I-squared statistic

MBNL1 – Muscleblind-like Splicing Regulator 1

PI – Prediction Interval

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Q – Cochran's Q statistic

REML – Restricted Maximum Likelihood

RNA – Ribonucleic Acid

RR – Relative Risk

SIR – Standardised Incidence Ratio

τ^2 (Tau^2) – Between-study Variance

Declarations

- **Ethics approval and consent to participate.**

  Human Ethics and Consent to Participate declarations: not applicable .

- **Consent for publication**

  Not applicable.

- **Availability of data and materials**

  The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

- **Competing interests**

  The authors declare that they have no competing interests.

  JMcC has received honoraria for speaking from UCB, Genzyme, and Argenix pharmaceuticals.

- **Funding**

  None

Acknowledgements

We are grateful to Richard Fallis, Librarian, Queen's University, Belfast, for designing and conducting the search strategy.
J McConville is very grateful to Mr K McNeany for supporting his academic work.

References

Abbott, D., N. E. Johnson, and L. A. Cannon-Albright. 2016. 'A population-based survey of risk for cancer in individuals diagnosed with myotonic dystrophy', *Muscle Nerve*, 54: 783-5.

Alsaggaf, R., R. M. Pfeiffer, E. E. Pearce, M. H. Greene, H. Lochmuller, and S. M. Gadalla. 2025. 'Mortality Trends and Causes of Death in Myotonic Dystrophy Type 1 Patients From the UK Clinical Practice Research Datalink', *Muscle Nerve*, 71: 229-36.

Bañuls, J., R. Botella, F. Palau, R. Ramón, C. Díaz, A. Payá, L. Carnero, and G. Vergara. 2004. 'Tissue and tumor mosaicism of the myotonin protein kinase gene trinucleotide repeat in a patient with multiple basal cell carcinomas associated with myotonic dystrophy', *J Am Acad Dermatol*, 50: S1-3.

Brook, J. D., M. E. McCurrach, H. G. Harley, A. J. Buckler, D. Church, H. Aburatani, K. Hunter, V. P. Stanton, J. P. Thirion, T. Hudson, and et al. 1992. 'Molecular basis of myotonic dystrophy: expansion of a trinucleotide (CTG) repeat at the 3' end of a transcript encoding a protein kinase family member', *Cell*, 69: 385.

Chiaramonti, A., and R. S. Gilgor. 1978. 'Pilomatricomas associated with myotonic dystrophy', *Arch Dermatol*, 114: 1363-5.

Ciriacks, K., D. Knabel, and M. B. Waite. 2020. 'Syndromes associated with multiple pilomatricomas: When should clinicians be concerned?', *Pediatr Dermatol*, 37: 9-17.

Emparanza, J. I., A. López de Munain, M. H. Greene, A. Matheu, R. Fernández-Torrón, and S. M. Gadalla. 2018. 'Cancer phenotype in myotonic dystrophy patients: Results from a meta-analysis', *Muscle Nerve*, 58: 517-22.

Fernández-Torrón, R., M. García-Puga, J. I. Emparanza, M. Maneiro, A. M. Cobo, J. J. Poza, J. B. Espinal, M. Zulaica, I. Ruiz, L. Martorell, D. Otaegui, A. Matheu, and A. López de Munain. 2016. 'Cancer risk in DM1 is sex-related and linked to miRNA-200/141 downregulation', *Neurology*, 87: 1250-7.

311 Gadalla, S. M., M. Lund, R. M. Pfeiffer, S. Gørtz, C. M. Mueller, R. T. Moxley, 3rd, S. Y. Kristinsson,
312 M. Björkholm, F. M. Shebl, J. E. Hilbert, O. Landgren, J. Wohlfahrt, M. Melbye, and M. H.
313 Greene. 2011. 'Cancer risk among patients with myotonic muscular dystrophy', *Jama*,
314 306: 2480-6.
315 Hameed, B., M. Ahmadzada, T. S. McNeel, D. B. DiCapua, and S. M. Gadalla. 2025. 'A novel
316 discovery of elevated risk of neuroendocrine tumors in patients with myotonic
317 dystrophy', *J Neurol Sci*, 478: 123722.
318 Ho, T. H., B. N. Charlet, M. G. Poulos, G. Singh, M. S. Swanson, and T. A. Cooper. 2004.
319 'Muscleblind proteins regulate alternative splicing', *Embo j*, 23: 3103-12.
320 Kinoshita, M., A. Igarashi, T. Komori, H. Tamura, M. Hayashi, K. Kinoshita, T. Deguchi, and K.
321 Hirose. 1997. 'Differences in CTG triplet repeat expansions in an ovarian cancer and cyst
322 from a patient with myotonic dystrophy', *Muscle Nerve*, 20: 622-4.
323 Kinoshita, M., R. Osanai, M. Kikkawa, A. Adachi, T. Ohtake, T. Komori, K. Hashimoto, S. Itoyama,
324 T. Mitarai, and K. Hirose. 2002. 'A patient with myotonic dystrophy type 1 (DM 1)
325 accompanied by laryngeal and renal cell carcinomas had a small CTG triplet repeat
326 expansion but no somatic instability in normal tissues', *Intern Med*, 41: 312-8.
327 Mahadevan, M., C. Tsilfidis, L. Sabourin, G. Shutler, C. Amemiya, G. Jansen, C. Neville, M.
328 Narang, J. Barceló, K. O'Hoy, and et al. 1992. 'Myotonic dystrophy mutation: an unstable
329 CTG repeat in the 3' untranslated region of the gene', *Science*, 255: 1253-5.
330 Mathieu, J., P. Allard, L. Potvin, C. Prévost, and P. Bégin. 1999. 'A 10-year study of mortality in a
331 cohort of patients with myotonic dystrophy', *Neurology*, 52: 1658-62.
332 Maya-González, C., G. Tettamanti, F. Taylan, A. Skarin Nordenvall, T. Sejersen, and A. Nordgren.
333 2024. 'Cancer Risk in Patients With Muscular Dystrophy and Myotonic Dystrophy: A
334 Register-Based Cohort Study', *Neurology*, 103: e209883.

Mesa-Álvarez, L., A. Batalla, Á Iglesias-Puzas, C. Álvarez, and Á Flórez. 2019. 'Multiple Pilomatricomas: A Retrospective Study and Literature Review', *Am J Dermatopathol*, 41: 293-95.

Mohamed, S., L. Pruna, and P. Kaminsky. 2013. '[Increasing risk of tumors in myotonic dystrophy type 1]', *Presse Med*, 42: e281-4.

Morales, F., E. Corrales, M. Vásquez, B. Zhang, H. Fernández, F. Alvarado, S. Cortés, C. Santamaría-Ulloa, Mmdbd Initiative-Mmdbdi, R. Krahe, and D. G. Monckton. 2023. 'Individual-specific levels of CTG•CAG somatic instability are shared across multiple tissues in myotonic dystrophy type 1', *Hum Mol Genet*, 32: 621-31.

Morales, F., M. Vásquez, E. Corrales, R. Vindas-Smith, C. Santamaría-Ulloa, B. Zhang, M. Sirito, M. R. Estecio, R. Krahe, and D. G. Monckton. 2020. 'Longitudinal increases in somatic mosaicism of the expanded CTG repeat in myotonic dystrophy type 1 are associated with variation in age-at-onset', *Hum Mol Genet*, 29: 2496-507.

Saponaro, G., E. De Paolis, M. Todaro, F. Azzuni, G. Gasparini, A. Bosso, G. Ascani, A. Minucci, and A. Moro. 2025. 'Pilomatricoma in Syndromic Contexts: A Literature Review and a Report of a Case in Apert Syndrome', *Dermatopathology (Basel)*, 12.

Seo, I., and J. M. Park. 2024. 'Myotonic dystrophy type 1 in South Korea: a comprehensive analysis of cancer and comorbidity risks', *Neurol Sci*, 45: 4573-81.

Wang, Y., R. M. Pfeiffer, R. Alsaggaf, W. Meeraus, J. C. Gage, L. A. Anderson, R. C. Bremer, N. Nikolenko, H. Lochmuller, M. H. Greene, and S. M. Gadalla. 2018. 'Risk of skin cancer among patients with myotonic dystrophy type 1 based on primary care physician data from the U.K. Clinical Practice Research Datalink', *Int J Cancer*, 142: 1174-81.

Win, A. K., P. G. Perattur, J. S. Pulido, C. M. Pulido, and N. M. Lindor. 2012. 'Increased cancer risks in myotonic dystrophy', *Mayo Clin Proc*, 87: 130-5.

Zhang, W., V. Bhandaru, N. E. Johnson, A. Moore, A. Lyons, R. Berry, C. Westfield, D. McMahon, A. Soim, B. Cai, and S. McDermott. 2025. 'Elevated Cancer Prevalence Identified at

Specific Anatomical Sites Among People With Myotonic Dystrophy Using a Population-Based Sample', *Muscle Nerve*, 72: 570-79.

Table 1: Summary of Studies Included in Systematic Review

First Author	Year	PMID	Country	Data Source	Study design	Total Number of DM patients (Number DM1 Patients included)	Person-Years	Cancer Cases (n)	Effect Measure	Analysis
Gadalla	2011	22166607	Sweden & Denmark	National hospital patient and cancer registries	Registry-based	1,658 (unknown)	14,170	104	SIR	**Meta-analysis**
Win	2012	22237010	USA	Mayo Clinic, Rochester medical records and national cancer registry	Population-based	307 (221)	Not reported	53	SIR	**Meta-analysis**
Mohamed	2013	23477718	France	Neuromuscular clinic review list and national cancer statistics	Population-based	109 (109)	Not reported	14	RR	Narrative
Abbott	2016	27064430	USA (Utah)	Utah Population Database	Population-based	281 (unknown)	Not reported in paper	17	RR	Narrative
Fernández-Torrón	2016	27558368	Spain	National DM1 cohort	Cohort study	424 (424)	18.796	27	SIR	**Meta-analysis**
Wang	2018	29114849	UK	Clinical Practice Research Datalink (CPRD)	Matched cohort	1,061 (1,061)	90,445	35	HR	Narrative (cohort overlap)
Alsaggaf	2018	30556050	United Kingdom	Clinical Practice Research Datalink (CPRD)	Matched cohort	927 (927)	140,554	41	HR	Narrative
Seo	2024	38613590	South Korea	National Health Insurance Database	Population-based	3323 (3,323)	14,164	400	SIR	**Meta-analysis**
Maya-González	2024	39233279	Sweden	National Patient Register + Cancer Register	Population-based	1,968 (unknown)	Not reported in paper	158	HR	Narrative (cohort overlap)
Hameed	2025	41100969	USA	Clinic and CA Registry-based cohort	Clinic and registry	211 (167)	Not reported	28	SIR	**Meta-analysis**
Zhang	2025	40586148	USA	MD STARnet population-based cohort	Cross-sectional/registry analysis	1,229 (1,114)	N/A	52	SPR	**Meta-analysis**

Studies reporting standardised incidence ratios (SIRs) were included in quantitative meta-analysis. Studies reporting hazard ratios (HRs), rate ratios (RRs), prevalence ratios, or overlapping cohorts were synthesised narratively.

Many studies identified patients using diagnostic codes which did not allow type of Myotonic dystrophy (1 or 2) to be identified. These were listed as unknown number of DM1 patients. Some studies reported containing DM1 patients only. Alsagaff et al. And Wang et al. Did not specify how inclusion of DM1 patients only was determined. Fernandez-Torron included molecularly confirmed DM1 patients only. Mohamed et al. Included only DM1 patients including 92 molecularly confirmed DM1 patients. Seo et al. Report diagnostic codes used to identify patients do not allow distinction for type of DM, however, report DM type 2 is not seen in South Korea. Win et al. Reported 118 DM1 patients and 103 unknown type DM, unknown DM type was assumed to be DM1 patients due to higher prevalence. Similarly, Zhang et al. Reported 1,001 DM1 patients and 113 unspecified DM type, unknown DM type was assumed to be DM1 patients due to higher prevalence.

Figure 1

Prisma Diagram

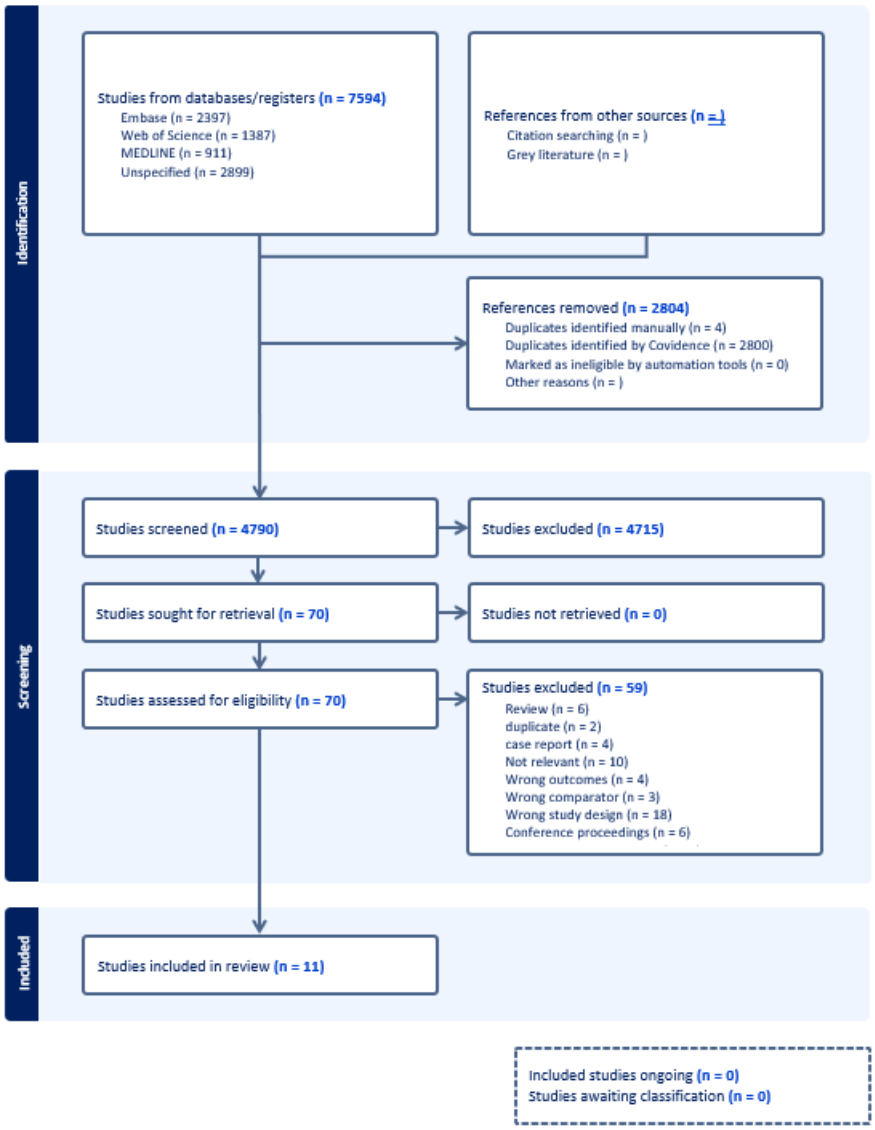
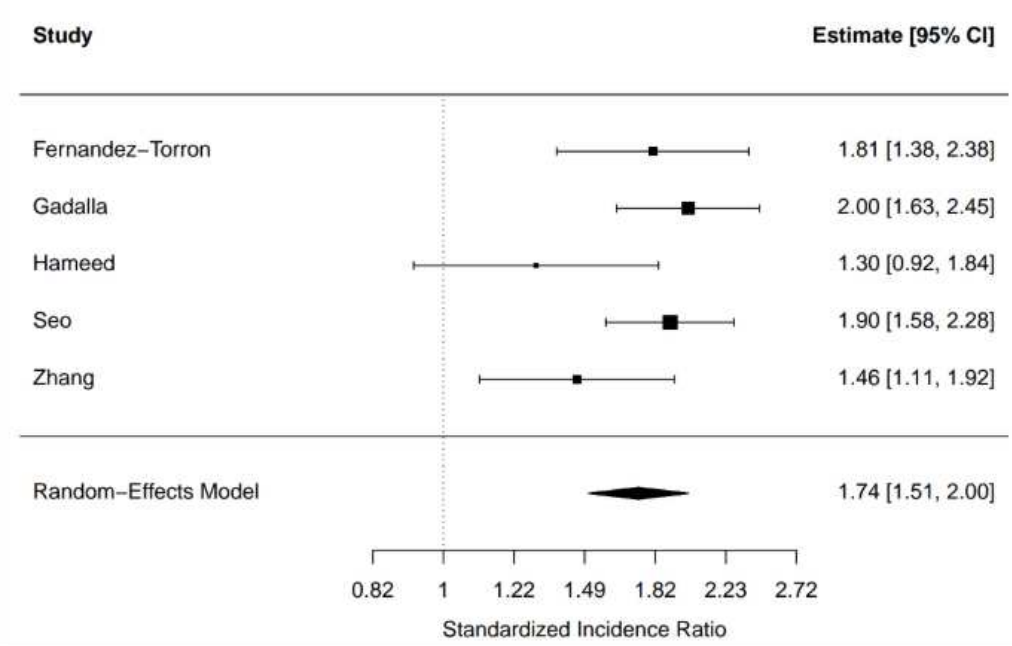


Figure 2

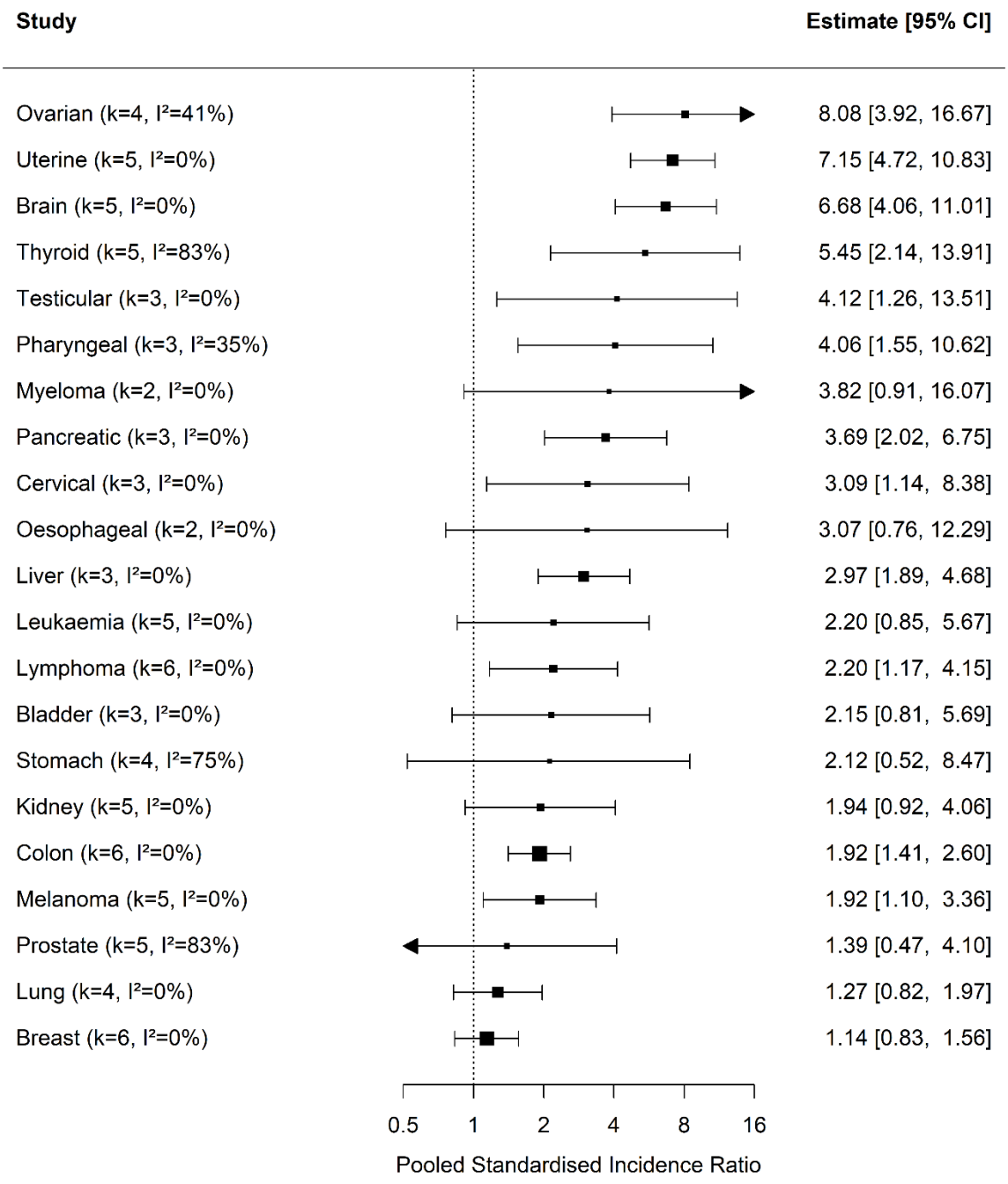
Pooled estimate of SIR for All cancers.



Forest Plot 1: Pooled estimate of SIR for All cancers

436 Figure 3

437 **Pooled estimate by cancer site in descending order of point estimate.** Pooled SIR and 95%
438 confidence interval. Number studies included, k; heterogeneity measure, I^2. Lower 95%
439 confidence interval exceeded 1 in 12/21 sites. Ovary, uterus, brain, thyroid, testis, pharynx,
440 pancreas, cervix, liver, lymphoma, colon and melanoma. Some common tumours were not
441 associated with increased cancer risk: prostate, lung and breast.



442

443 Figure 4

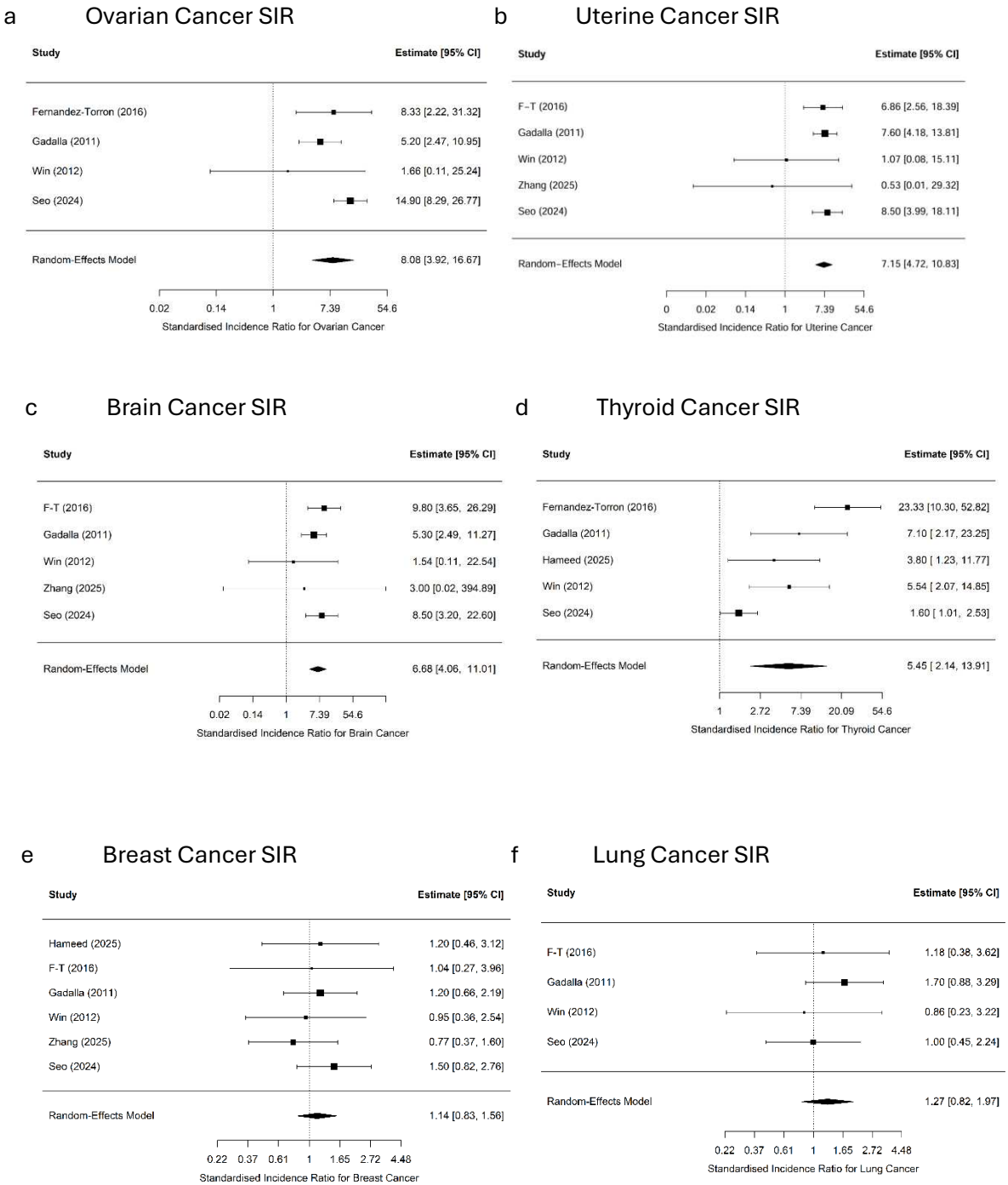
444 **Selected Forest Plots.** a-d, sites of highest pooled SIR effect size for cancer risk in DM1. e&f,

445 sites of lowest effect size.

446

447

448



Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementASearchstrategy.docx
- SupplementaryFiguresAUForestPlotsandHRTables.docx
- SupplementaryTableS1NOSS2Overlap.docx
- SupplementaryTableS3SummaryStats.docx
- SupplementaryFigureS4SingleStudyRates.docx