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Evidence-based guidelines

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International Guideline for Idiopathic Inflammatory Myopathy-Associated Cancer Screening: an International Myositis Assessment and Clinical Studies Group (IMACS) initiative

A list of authors and their affiliations appears at the end of the paper

Abstract

Adult-onset idiopathic inflammatory myopathy (IIM) is associated with an increased cancer risk within the 3 years preceding and following IIM onset. Evidence- and consensus-based recommendations for IIM-associated cancer screening can potentially improve outcomes. This International Guideline for IIM-Associated Cancer Screening provides recommendations addressing IIM-associated cancer risk stratification, cancer screening modalities and screening frequency. The international Expert Group formed a total of 18 recommendations via a modified Delphi approach using a series of online surveys. First, the recommendations enable an individual patient's IIM-associated cancer risk to be stratified into standard, moderate or high risk according to the IIM subtype, autoantibody status and clinical features. Second, the recommendations outline a 'basic' screening panel (including chest radiography and preliminary laboratory tests) and an 'enhanced' screening panel (including CT and tumour markers). Third, the recommendations advise on the timing and frequency of screening via basic and enhanced panels, according to risk status. The recommendations also advise consideration of upper or lower gastrointestinal endoscopy, nasoendoscopy and ^{18}F-FDG PET–CT scanning in specific patient populations. These recommendations are aimed at facilitating earlier IIM-associated cancer detection, especially in those who are at a high risk, thus potentially improving outcomes, including survival.

Sections

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Introduction

Idiopathic inflammatory myopathy (IIM, commonly termed 'myositis') is a chronic multisystem autoimmune condition with a range of manifestations, including muscle inflammation, skin involvement and interstitial lung disease[1,2]. Adult-onset IIM is associated with an increased risk of cancer, particularly within the 3 years prior to and the 3 years after IIM onset[3]. Evidence suggests that up to one in four people with IIM are diagnosed with cancer within 3 years of IIM onset[4]. Various cancers have been reported, including lung, ovarian, colorectal, lymphoma, breast and nasopharyngeal cancers among the most common forms[5]. Cancer remains the leading cause of death in adults with IIM[4,6–8], likely due in part to delayed diagnosis. IIM-associated cancers are overwhelmingly diagnosed at an advanced stage; a cohort study identified that 83% of IIM-associated cancers were stage III or IV at the time of diagnosis and were associated with a cancer remission rate of only 17%[5].

Early detection of cancer is key to improving outcomes. Consensus-based recommendations, based on the available evidence, will inform screening for malignancy in patients with IIM and standardize practices across health systems, particularly for patients managed outside specialist IIM centres.

The International Myositis Assessment and Clinical Studies Group (IMACS), the largest international multidisciplinary group for IIM scientific studies, sponsored a project to develop evidence- and consensus-based cancer screening recommendations for patients with IIM. The first component of the project involved conducting a meta-analysis, which was aimed at identifying IIM-associated cancer risk factors, and a systematic review, which was aimed at compiling evidence on screening modalities[9]. The second component of work involved forming an international multidisciplinary Expert Group with expertise in IIM and cancer screening, with the aim of developing evidence-based consensus recommendations on screening for IIM-associated cancer, specifically addressing cancer risk stratification, screening modalities and screening frequency. Herein, we present the methodology and consensus-based recommendations for IIM-associated cancer screening developed by the large multidisciplinary international Expert Group derived from members of the IMACS. These recommendations have been scientifically reviewed by the IMACS Scientific Committee and have been endorsed by the International Myositis Society. They will be revised and endorsed periodically.

Methods

The recommendation formation process was guided by a Steering Committee (A.G.S.O., J.P.C., H.C., L.C., D.F., P.G., P.M.M., N.M., A.S.-O., J.S., S.L.T., R.A.V., V.P.W. and R.A.), formed by IIM specialists affiliated with the IMACS, led by R.A. and A.G.S.O.

Evidence collation was carried out via a systematic literature review (SLR) to update the meta-analysis and systematic review published in 2019[9] using the same methodology (with regard to study selection, data extraction, quality assessment and data synthesis) and adhering to 'Preferred reporting items for systematic reviews and meta-analyses' guidelines[10] (see Acknowledgements section for details of the individuals who provided input on the SLR and meta-analysis). Evidence published prior to 1 April 2022 was included.

An international Expert Group with expertise in IIM and cancer screening was convened. Eligibility criteria for the Expert Group included clinical expertise in IIM with ≥10 years' experience, or one or more publications focused on clinically translational aspects of IIM-associated cancer, or clinical and/or research expertise in non-IIM-associated cancer screening. The Expert Group comprised 75 individuals, including members of the Steering Committee but excluding the process leads R.A. and A.G.S.O. The Expert Group comprised 46 rheumatologists, 12 neurologists, 9 dermatologists, 3 oncologists with expertise in cancer screening, 2 pulmonologists with a special interest in IIM, 2 researchers with expertise in cancer screening implementation and 1 paediatric rheumatologist, from 22 countries across five continents (North America, South America, Europe, Asia and Australia) (see Supplementary Table 1 for the composition of the Expert Group by specialty and geographical location). The full list of members of the International Myositis Assessment and Clinical Studies Group Cancer Screening Expert Group is included in the authorship list.

The recommendation formation process followed a modified Delphi Method approach using a series of online surveys. Expert Group members were advised to review the evidence contained within the updated SLR and the published meta-analysis[9] prior to completing the first survey. The first survey, created by A.G.S.O and R.A. and amended by the Steering Committee, was aimed at identifying the opinion of the Expert Group regarding IIM-associated cancer risk factors (that is, factors that are associated with increased cancer risk compared with the wider IIM population), 'protective factors' (that is, factors that are associated with reduced cancer risk compared with the wider IIM population) and appropriate use of cancer screening modalities. The questions comprising the first survey are detailed in Supplementary Tables 2–4. The Steering Committee created draft recommendations based on responses from the first survey.

Members of the Expert Group were asked to consider individualized cancer risk stratification in comparison with the wider IIM population only, not the general population.

Subsequent surveys asked members of the Expert Group to rate their level of agreement with each draft recommendation on a 1–9 numerical rating scale (with 1 indicating 'complete disagreement' and 9 'complete agreement'). The median vote rating for each draft recommendation was calculated and defined a priori as 'disagreement' (median vote of 1–3), 'uncertainty' (median vote of 4–6) or 'consensus' (median vote of 7–9). Expert Group members were able to provide feedback to A.G.S.O. and R.A. on each recommendation. Draft recommendations were amended according to vote ratings and the feedback provided by Expert Group members, and were then re-presented to the Expert Group via an online survey. A total of three recommendation voting surveys, in addition to the preliminary survey, were carried out before consensus was reached (see Supplementary Tables 5–8).

Each recommendation was assigned a strength of recommendation of strong (1) or conditional (2); 'strong' recommendations were made where the benefits are deemed to clearly outweigh the risks, whereas 'conditional' recommendations were made when the benefits are more balanced with the risks.

Each recommendation was assigned a quality of supporting evidence via the Scottish Intercollegiate Guidelines Network[11], thus summarizing the quality of the body of evidence for each recommendation as high (A), moderate (B), low (C) or very low (D), according to Grading of Recommendations, Assessment, Development, and Evaluations methodology.

Three patient partners with adult-onset IIM provided written feedback on the acceptability of the final recommendations and co-authored the final manuscript, although they were not involved in the voting process (one patient partner chose to remain anonymous and not be included as a co-author).

The project and final manuscript were reviewed and approved by the IMACS Scientific Committee.

Recommendations

A total of 18 final recommendations were formed, which address IIM-associated cancer risk stratification (compared with the wider IIM population, not the general population), use of screening modalities and screening frequency. The recommendations are discussed below and summarized in Table 1. The statement for each recommendation is followed by details relating to the strength of recommendation, quality of the supporting evidence (Grading of Recommendations, Assessment, Development, and Evaluations level A–D), the number of votes and the median vote rating with the interquartile range (IQR).

Regarding strength of recommendation, 13 recommendations are strong and 5 are conditional. The quality of supporting evidence was moderate (B) for 8 recommendations, low (C) for 4 recommendations and very low (D) for 3 recommendations; 3 further recommendations had no corresponding evidence base and were formed via expert consensus only. No recommendation had high (A) quality of supporting evidence. The evidence corresponding to each recommendation is available in Supplementary Table 9.

Recommendation 1. Screening for IIM-associated cancer is not routinely required in patients with juvenile-onset IIM

- Strong recommendation.
- Evidence level: B.
- Voting: 62 votes, median vote rating 8 (IQR 8–9).

Current evidence indicates that cancer risk is not increased in patients with juvenile-onset IIM in comparison with the general population[12–18]. Therefore, routine cancer screening in this patient group was not deemed necessary by the Expert Group. Clinicians should, however, be vigilant for features suggestive of underlying cancer in patients with juvenile-onset IIM, including abnormal complete blood count, unexplained weight loss, fevers, and splenomegaly and/or lymphadenopathy.

Recommendation 2. Screening for IIM-associated cancer is not routinely required in patients with verified inclusion body myositis

- Strong recommendation.
- Evidence level: B.
- Voting: 62 votes, median vote rating 8 (IQR 7–9).

Existing evidence indicates that inclusion body myositis (IBM) is not associated with an increased risk of cancer[4,19]. In particular, a nationwide Norwegian-based cohort study by Dobloug et al. calculated a cancer standardized incidence rate of 1.0 (95% CI 0.6–2.1) in 100 cases of IBM, indicating a cancer risk similar to that of the general population[4]. However, emerging evidence suggests a potential association between IBM and T cell large granular lymphocytic leukaemia[20,21]; ongoing research could further delineate this association and potentially inform the need for screening.

Recommendation 3. All patients with IIM, irrespective of cancer risk, should continue to participate in country- or region-specific age- and sex-appropriate cancer screening programmes

- Strong recommendation.
- Evidence level: B.
- Voting: 64 votes, median vote rating 9 (IQR 9–9).

It is imperative that all patients with IIM, including those with juvenile-onset IIM and IBM, continue to participate in population-level cancer screening programmes, such as mammography for breast cancer, pelvic examination and/or cervical screening (smear test) for cervical cancer and low radiation dose chest CT scanning for lung cancer, as available in their country or region according to their age and sex[22]. These recommendations are aimed at facilitating the detection of IIM-associated cancers above and beyond the general population screening guidelines. Moreover, these recommendations are not tailored to detect cancers that might occur because of non-IIM-associated risk factors for which certain countries or regions might have instigated screening programmes.

Recommendation 4. All adult patients with new-onset IIM should be tested for myositis-specific autoantibodies and myositis-associated autoantibodies to assist stratification of cancer risk

- Strong recommendation.
- Evidence level: B.
- Voting: 64 votes, median vote rating 9 (IQR 8–9).

Myositis-specific autoantibodies (MSA) can aid risk stratification for IIM-associated cancer, diagnosis and prediction of clinical manifestations and aid management decisions. A variety of methods are available for MSA detection and clinicians should interpret the results of such tests in the context of potential limitations, especially false positivity or false negativity.

Recommendation 5. Underlying cancer risk of patients with adult-onset IIM should be stratified according to IIM subtype, autoantibody status and clinical features

- Strong recommendation.
- Evidence level: B.
- Voting: 52 votes, median vote rating 8 (IQR 7–9).

The Expert Group identified IIM subtypes, autoantibodies and clinical features associated with high, intermediate and low risk of IIM-associated cancer.

'High risk' factors.

- Dermatomyositis
- Anti-transcriptional intermediary factor 1γ (anti-TIF1γ) antibody positivity
- Anti-nuclear matrix protein 2 (anti-NXP2) antibody positivity
- Age >40 years at the time of IIM onset
- Features of persistent high disease activity despite immunosuppressive therapy (including relapse of previously controlled disease)
- Dysphagia (moderate to severe)
- Cutaneous necrosis or ulceration

'Intermediate risk' factors.

- Clinically amyopathic dermatomyositis (CADM)
- Polymyositis
- Immune-mediated necrotizing myopathy (IMNM)
- Anti-small ubiquitin-like modifier-1 activating enzyme (anti-SAE1) antibody positivity
- Anti-3-hydroxy 3-methylutaryl coA reductase (anti-HMGCR) antibody positivity

Table 1 | Summary of all recommendations from the International Guideline for IIM-Associated Cancer Screening

Recommendation	Strength	Level of evidence[a]	Consensus	
			Number of votes	Median score (IQR)
1. Screening for IIM-associated cancer is not routinely required in patients with juvenile-onset IIM	Strong	Moderate	62	8 (8–9)
2. Screening for IIM-associated cancer is not routinely required in patients with verified inclusion body myositis	Strong	Moderate	62	8 (7–9)
3. All patients with IIM, irrespective of cancer risk, should continue to participate in country- or region-specific age- and sex-appropriate cancer screening programmes	Strong	Moderate	64	9 (9–9)
4. All adult patients with new-onset IIM should be tested for myositis-specific autoantibodies and myositis-associated autoantibodies to assist stratification of cancer risk	Strong	Moderate	64	9 (8–9)
5. Underlying cancer risk of patients with adult-onset IIM should be stratified according to IIM subtype, autoantibody status and clinical features in the following manner: **High risk:** Dermatomyositis Anti-TIF1γ antibody positivity Anti-NXP2 antibody positivity Age >40 years at the time of IIM onset Features of persistent high disease activity despite immunosuppressive therapy (including relapse of previously controlled disease) Dysphagia (moderate to severe) Cutaneous necrosis or ulceration **Intermediate risk:** CADM Polymyositis IMNM Anti-SAE1 antibody positivity Anti-HMGCR antibody positivity Anti-Mi2 antibody positivity Anti-MDA5 antibody positivity Male sex **Low risk:** ASSD Overlap IIM–CTD-associated myositis Anti-SRP antibody positivity Anti-Jo1 antibody positivity Non-Jo1 ASSD antibody positivity Myositis-associated antibody positivity (anti-PM-Scl, anti-Ku, anti-RNP, anti-SSA/Ro, anti-SSB/La antibodies) Raynaud phenomenon Inflammatory arthropathy Interstitial lung disease	Strong	Moderate	52	8 (7–9)
6. Patients with adult-onset IIM who have two or more 'high risk' factors (subtype, autoantibody or clinical feature) should be considered to be at a 'high risk of IIM-related cancer'[b]	Strong	Moderate	67	8 (8–9)
7. Patients with adult-onset IIM who have two or more 'intermediate risk' factors (subtype, autoantibody or clinical feature) or only one 'high risk' factor (subtype, autoantibody or clinical feature) should be considered to be at a 'moderate risk of IIM-related cancer'[b]	Strong	Moderate	67	7 (7–9)
8. Patients with adult-onset IIM who do not fulfil the 'high' or 'moderate' risk definitions as outlined in recommendations 6 and 7 should be considered to be at a 'standard risk of IIM-related cancer'[b]	Strong	Moderate	67	8 (7–9)
9. 'Basic cancer screening' should include the following investigations (in addition to country- or region-specific age- and sex-appropriate cancer screening programmes for the general population): Comprehensive history Comprehensive physical examination Complete blood count Serum liver function tests Serum erythrocyte sedimentation rate and/or plasma viscosity Serum C-reactive protein Serum protein electrophoresis and measurement of free light chains Urinalysis Plain chest X-ray radiograph	Strong	Low	50	7 (6–8)

Table 1 (continued) | Summary of all recommendations from the International Guideline for IIM-Associated Cancer Screening

Recommendation	Strength	Level of evidence[a]	Consensus	
			Number of votes	Median score (IQR)
10. 'Enhanced cancer screening' should include the following investigations: CT scan of the neck, thorax, abdomen and pelvis Cervical screening[c] Mammography[c] Prostate-specific antigen blood test[c] CA-125 blood test Pelvic or transvaginal ultrasonography for ovarian cancer Faecal occult blood[c]	Strong	Low	51	8 (7–8)
11. Patients with adult-onset IIM at 'standard risk of IIM-related cancer' should undergo 'basic cancer screening' at the time of IIM diagnosis. This screening is in addition to country- or region-specific age- and sex-appropriate screening programmes for the general population	Strong	NA[d]	67	8 (7–9)
12. Patients with adult-onset IIM at 'moderate risk of IIM-related cancer' should undergo 'basic cancer screening' and 'enhanced cancer screening' at the time of IIM diagnosis	Strong	NA[d]	66	8 (7–9)
13. Patients with adult-onset IIM at a 'high risk of IIM-related cancer' should undergo 'enhanced cancer screening' and 'basic cancer screening' at the time of diagnosis and 'basic cancer screening' annually for 3 years	Strong	NA[d]	67	8 (7–9)
14. Clinicians should consider carrying out an ^{18}F-FDG PET–CT scan for patients with adult-onset IIM at a 'high risk of IIM-related cancer', where underlying cancer has not been detected by investigations at the time of IIM diagnosis	Conditional	Low	67	8 (7–9)
15. Clinicians should consider carrying out an ^{18}F-FDG PET–CT scan as a single screening investigation for patients with anti-TIF1γ antibody-positive dermatomyositis with disease onset at age >40 years and with ≥1 additional 'high risk' clinical feature	Conditional	Low	67	8 (7–9)
16. Clinicians should consider carrying out upper and lower gastrointestinal endoscopy for patients with adult-onset IIM at a 'high risk of IIM-related cancer', where underlying cancer has not been detected by investigations at the time of IIM diagnosis	Conditional	Very low	67	8 (7–9)
17. Clinicians should consider carrying out nasoendoscopy at the time of diagnosis in patients with adult-onset IIM in geographical regions where the risk of nasopharyngeal carcinoma is increased	Conditional	Very low	67	8 (7–9)
18. Clinicians should consider cancer screening in all patients with IIM with the following 'red flag' symptoms or clinical features, regardless of risk category: Unintentional weight loss Family history of cancer Smoking Unexplained fever Night sweats	Conditional	Very low	66	9 (7–9)

^{18}F-FDG PET–CT, ^{18}F-fluoro-deoxy-glucose PET–CT; ASSD, anti-synthetase syndrome; CADM, clinically amyopathic dermatomyositis; HMGCR, 3-hydroxy 3-methylutaryl coenzyme A reductase; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; IQR, interquartile range; MDA5, melanoma differentiation-associated gene 5; NA, not applicable; NXP2, nuclear matrix protein 2; RNP, ribonucleoprotein; SAE1, small ubiquitin-like modifier-1 activating enzyme; SRP, signal recognition particle; TIF1γ, transcriptional intermediary factor 1γ. [a]According to Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) methodology, with evidence quality graded as high (A), moderate (B), low (C) or very low (D). [b]Risk categories are in comparison with the IIM population, not the general population. [c]If not already part of country- or region-specific age- and sex-appropriate screening programmes. [d]These recommendations had no corresponding evidence base and were formed via expert consensus only. Adapted with permission from ref. 41.

- Anti-Mi2 antibody positivity
- Anti-melanoma differentiation-associated gene 5 (anti-MDA5) antibody positivity
- Male sex

'Low risk' factors.

- Anti-synthetase syndrome (ASSD)
- Overlap IIM–connective tissue disease-associated myositis
- Anti-signal recognition particle (anti-SRP) antibody positivity
- Anti-Jo1 antibody positivity
- Non-Jo1 ASSD antibody positivity
- Myositis-associated antibody positivity (anti-PM-Scl, anti-Ku, anti-RNP, anti-SSA/Ro, anti-SSB/La antibodies)
- Raynaud phenomenon
- Inflammatory arthropathy
- Interstitial lung disease

Recommendation 6. Patients with adult-onset IIM who have two or more 'high risk' factors (subtype, autoantibody or clinical feature) should be considered to be at a 'high risk of IIM-related cancer'

- Strong recommendation.
- Evidence level: B.
- Voting: 67 votes, median vote rating 8 (IQR 8–9).

Recommendation 7. Patients with adult-onset IIM who have two or more 'intermediate risk' factors (subtype, autoantibody or clinical feature) or only one 'high risk' factor (subtype, autoantibody or clinical feature) should be considered to be at a 'moderate risk of IIM-related cancer'

- Strong recommendation.
- Evidence level: B.
- Voting: 67 votes, median vote rating 7 (IQR 7–9).

Recommendation 8. Patients with adult-onset IIM who do not fulfil the 'high' or 'moderate' risk definitions as outlined in recommendations 6 and 7 should be considered to be at a 'standard risk of IIM-related cancer'

- Strong recommendation.
- Evidence level: B.
- Voting: 67 votes, median vote rating 8 (IQR 7–9).

These recommendations have been formed to enable clinicians to stratify an individual patient's risk of IIM-associated cancer. The Expert Group formed an initial recommendation that identifies IIM subtypes, autoantibodies and clinical features associated with 'high', 'intermediate' and 'low' risk of IIM-associated cancer (Box 1). The Expert Group also formed three subsequent recommendations that enable clinicians to assign an individual patient as having an overall 'high', 'moderate' or 'standard' risk of IIM-associated cancer, on the basis of their IIM subtype, autoantibody status and clinical features. It is important to note that these risk categories are in comparison with the overall IIM population, not the general population; indeed, those with a 'standard' risk of IIM-associated cancer will likely have an increased risk of cancer compared with the general population. Empirical comparison of cancer risk between the standard risk group and the general population has not yet been carried out and is clearly warranted.

Box 1

Examples of IIM-associated cancer risk stratification

Example 1:
A 70-year-old woman with anti-NXP2 antibody-positive dermatomyositis, who had initially developed symptoms 6 months previously, would be classified as being at a 'high' risk, owing to fulfilment of three individual 'high risk' factors: dermatomyositis, anti-NXP2 antibody positivity and age >40 years at the time of IIM onset.

Example 2:
A 52-year-old woman with anti-HMGCR antibody-positive immune-mediated necrotizing myopathy, who had developed symptoms 3 months previously, would be classified as being at a 'moderate' risk, owing to fulfilment of two individual intermediate risk factors: immune-mediated necrotizing myopathy and anti-HMGCR antibody positivity.

Example 3:
A 26-year-old man with anti-Jo1-positive anti-synthetase syndrome, who had developed symptoms 2 months previously, would be classified as being at a 'standard' risk, owing to non-fulfilment of 'moderate' or 'high risk' criteria.

HMGCR, 3-hydroxy 3-methylutaryl coA reductase; IIM, idiopathic inflammatory myopathy; NXP2, nuclear matrix protein 2.

Factors associated with a high risk of IIM-related cancer. The Expert Group identified seven 'high risk' factors (one subtype, two autoantibodies and four clinical features). Dermatomyositis is consistently associated with the highest cancer risk, compared with other IIM subtypes; our 2019 meta-analysis identified a risk ratio (RR) of 2.21 (95% CI 1.78–2.77), indicating that the risk of cancer with dermatomyositis is more than double that with other IIM subtypes[9]. A large number of observational studies exist that detail cancer risk for each IIM subtype. A large body of evidence has characterized the high cancer risk associated with anti-TIF1γ antibody positivity, hence its inclusion as a high risk factor with a RR of 4.68, indicating that the risk of cancer is over four times higher for adults with anti-TIF1γ antibody-positive IIM than for those with anti-TIF1γ antibody-negative IIM. Anti-NXP2 antibody positivity has also been associated with an increased risk of cancer; however, this risk is considered lower than that associated with anti-TIF1γ antibody positivity. It is important to note that a number of studies associating anti-NXP2 antibody positivity with an increased risk of cancer employed the general population, not an IIM cohort, as a comparator group[23,24]. Our 2019 meta-analysis, which employed the wider IIM cohort as a comparator group, identified no association of anti-NXP2 antibody positivity with cancer (RR 1.16, 95% CI 0.73–1.87)[9]. However, the Expert Group deemed the available evidence sufficient to categorize anti-NXP2 antibody positivity as a 'high risk' factor.

Older age at time of IIM onset is associated with increased cancer risk. Selection of a specific age threshold is challenging owing to the probable incremental risk that older age of IIM-onset confers; a threshold of 40 years was chosen owing to the clear age cut-off for cancer development identified in studies of anti-TIF1γ antibody-positive adults[25,26]. It is important to note that no clear age cut-off has been established in the context of other autoantibody profiles and an incremental risk with increasing age is likely; however, the 40-year threshold was selected for clarity across all patients regardless of clinical features and autoantibody status. The accuracy of this age threshold will be assessed in future research into the utility of the guideline.

Features of persistent high disease activity despite immunosuppressive therapy were deemed by the Expert Group to be associated with a high risk of cancer. Evidence exists to support the relationship between persistent high disease activity, including myositis and skin involvement[27–29], and increased cancer risk, especially when associated with anti-TIF1γ antibody positivity; overall, however, the body of evidence is limited. Dysphagia, especially when treatment-refractory, has been associated with cancer, hence being deemed a 'high risk' factor by the Expert Group. The mechanism between dysphagia and increased IIM-associated cancer risk is not clear; however, dysphagia could represent a manifestation of persistent high disease activity. Finally, cutaneous necrosis and/or ulceration, which has been associated with increased risk of cancer, potentially owing to its association with severe refractory dermatomyositis, was deemed a 'high risk' factor by the Expert Group.

Factors associated with an intermediate risk of IIM-related cancer. Eight intermediate risk factors (three subtypes, four autoantibodies and one clinical feature) were identified by the Expert Group. The subtypes CADM, polymyositis and IMNM were assigned as being associated with an intermediate cancer risk; evidence suggests that the risk of cancer in these IIM subtypes is lower than that in dermatomyositis, but higher than that in ASSD and 'overlap IIM'. The definition of polymyositis is challenging, with studies in the past 5 years

indicating that some patients might be more appropriately classified as having other IIM subtypes such as IBM, IMNM or ASSD[30,31]. Polymyositis is still a commonly diagnosed condition; therefore, the Expert Group agreed to its inclusion as an 'intermediate' cancer risk factor. CADM is less commonly associated with cancer than dermatomyositis; however, the evidence base is limited. Overall, IMNM was classified as an intermediate cancer risk factor by the Expert Group. Recognizing the results of a study by Allenbach et al.[32], the Expert Group deemed it appropriate to distinguish cancer risk for patients with IMNM according to MSA positivity, with anti-HMGCR antibody positivity assigned as an 'intermediate' risk factor and anti-SRP antibody positivity a 'low' risk factor. The study by Allenbach et al.[32], however, identified different cancer risks for anti-SRP, anti-HMGCR and autoantibody-negative IMNM cohorts using the general population, not an IIM cohort, as a comparator group. Male sex and anti-MDA5, anti-Mi2 and anti-SAE1 antibody positivity were assigned as 'intermediate' risk factors by the Expert Group in light of the results of our meta-analysis[9]. In particular, anti-MDA5, anti-Mi2 and anti-SAE1 antibody positivity were assigned as intermediate risk factors owing to their non-significant association with cancer in the meta-analysis[9]. Defining MSA negativity is challenging owing to variations of testing techniques and ability to test for more recently identified MSAs across countries and health systems; therefore, MSA negativity was not included within risk stratification.

Factors associated with a low risk of IIM-related cancer. Nine 'low risk' factors (two subtypes, four autoantibodies, three clinical feature) were identified by the Expert Group. Our meta-analysis[9] and other evidence indicate a low risk of cancer for patients with ASSD, ASSD-associated clinical features (such as interstitial lung disease, inflammatory arthropathy and Raynaud phenomenon) and MSAs (such as anti-Jo1 antibodies), and for patients with overlap IIM or connective tissue disease-associated IIM.

Stratification of cancer risk. Three recommendations address estimation of the risk of IIM-associated cancer according to combinations of IIM subtype, clinical features and MSAs: patients with two 'high risk' factors are deemed to be at a high risk, patients with one 'high risk' factor or two 'intermediate risk' factors are deemed to be at a moderate risk, and the remainder are deemed to be at a standard risk. It is important to note that these combinations are based on expert opinion and available observational evidence, rather than empirical evidence quantifying cancer risk according to each combination. The examples of IIM-associated cancer risk stratification in individual patients in Box 1 illustrate the implementation of these recommendations.

Recommendation 9. 'Basic cancer screening' should include the following investigations (in addition to country- or region-specific age- and sex-appropriate cancer screening programmes for the general population): comprehensive history; comprehensive physical examination; complete blood count; serum liver function tests; serum erythrocyte sedimentation rate and/or plasma viscosity; serum C-reactive protein; serum protein electrophoresis and measurement of free light chains; urinalysis; and plain chest X-ray radiograph

- Strong recommendation.
- Evidence level: C.
- Voting: 50 votes, median vote rating 7 (IQR 6–8).

Recommendation 10. 'Enhanced cancer screening' should include the following investigations: CT scan of the neck, thorax, abdomen and pelvis; cervical screening; mammography; prostate-specific antigen blood test; CA-125 blood test; pelvic or transvaginal ultrasonography for ovarian cancer; faecal occult blood test

- Strong recommendation.
- Evidence level: C.
- Voting: 50 votes, median vote rating 7 (IQR 6–8).

Cervical screening, mammography, prostate-specific antigen (PSA) blood test, pelvic or trans-vaginal ultrasonography for ovarian cancer and faecal occult blood test should be included in 'enhanced cancer screening' if not already part of country- or region-specific age- and sex-appropriate screening programmes for the general population.

Recommendation 11. Patients with adult-onset IIM at a 'standard risk of IIM-related cancer' should undergo 'basic cancer screening' at the time of IIM diagnosis. This screening is in addition to country- or region-specific age- and sex-appropriate screening programmes for the general population

- Strong recommendation.
- No corresponding evidence base; recommendation formed via expert consensus only.
- Voting: 67 votes, median vote rating 8 (IQR 7–9).

Recommendation 12. Patients with adult-onset IIM at a 'moderate risk of IIM-related cancer' should undergo 'basic cancer screening' and 'enhanced cancer screening' at the time of IIM diagnosis

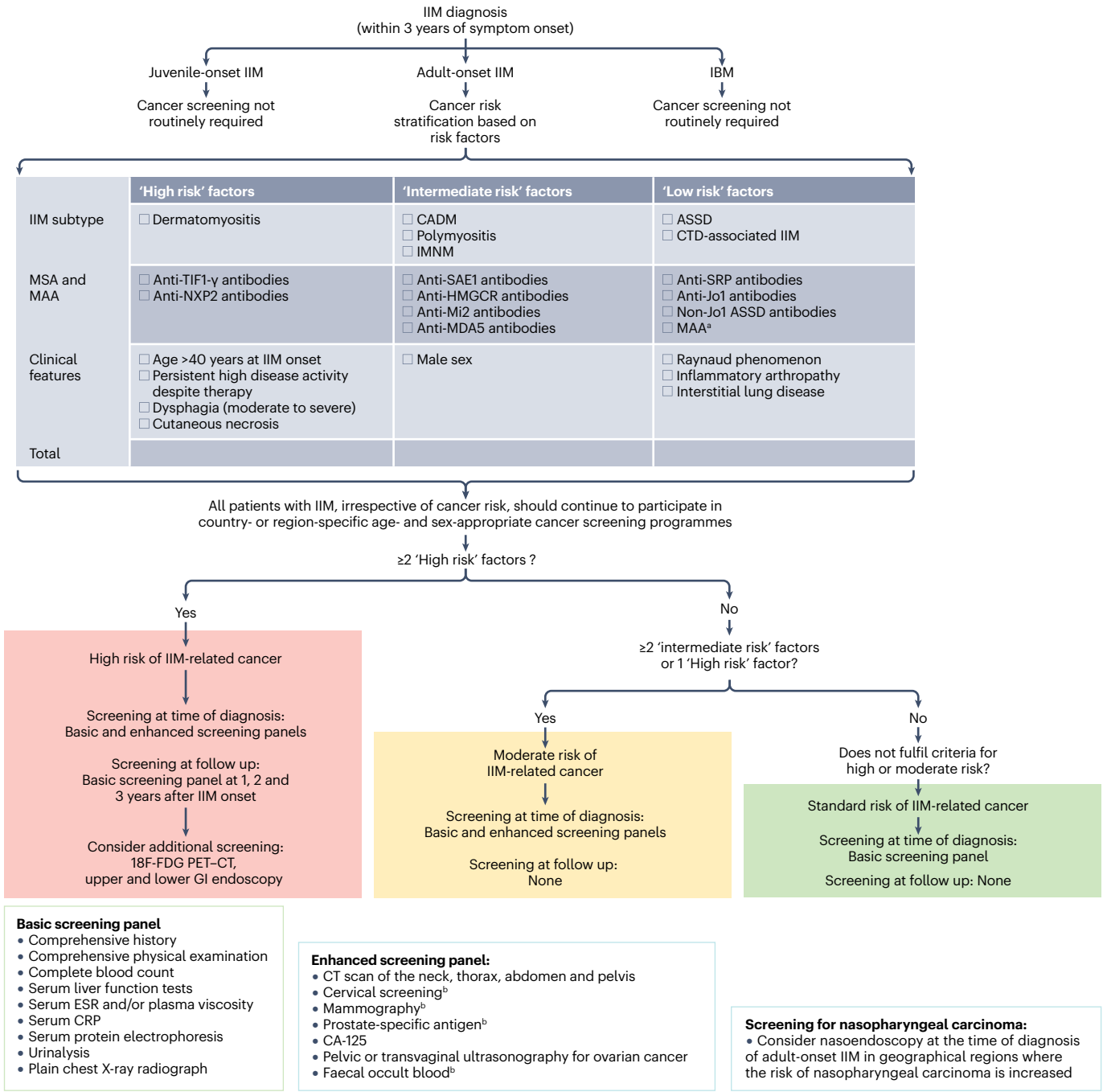
- Strong recommendation.
- No corresponding evidence base; recommendation formed via expert consensus only.
- Voting: 66 votes, median vote rating 8 (IQR 7–9).

Recommendation 13. Patients with adult-onset IIM at a 'high risk of IIM-related cancer' should undergo 'enhanced cancer screening' and 'basic cancer screening' at the time of diagnosis and 'basic cancer screening' annually for 3 years

- Strong recommendation.
- No corresponding evidence base; recommendation formed via expert consensus only.
- Voting: 67 votes, median vote rating 8 (IQR 7–9).

The Expert Group deemed it appropriate to form two panels of screening approaches — basic and enhanced — beyond age- and sex-based general population screening. The 'basic' screening panel is aimed at facilitating clinicians' ability to identify clinical features potentially consistent with IIM-associated cancer, such as iron deficiency anaemia indicating colon cancer, monoclonal gammopathy indicating multiple myeloma and chest X-ray radiograph-visible lung cancer.

The 'enhanced' screening panel was formulated to facilitate the identification of the most common IIM-associated cancers, such as breast, lung and ovarian cancer. Patients might have undergone a number of tests as part of country- or region-specific age- and sex-appropriate screening programmes, such as mammography or PSA level measurement; clinicians should balance the benefits of repeating such investigations against the risks on an individual patient basis in the context of cancer risk. Clinicians should also consider the potential



increased cancer risk due to investigations that involve radiation exposure, such as CT-based investigations.

The Expert Group formed recommendations relating to the timing and frequency of carrying out 'basic' and 'enhanced' screening according to IIM-associated cancer risk category (see Fig. 1 for a flowchart detailing risk stratification). Screening should be carried out for patients diagnosed within 3 years of IIM symptom onset; the recommendations therefore do not apply to those diagnosed after this time period. These recommendations are based on expert opinion only; no study has empirically investigated the utility of the timing and frequency of these specific panels of basic and enhanced cancer screening and hence the inability to ascribe an evidence quality grade.

Recommendation 14. Clinicians should consider carrying out an ^{18}F-FDG PET–CT scan for patients with adult-onset IIM at a 'high risk of IIM-related cancer', where underlying cancer has not been detected by investigations at the time of IIM diagnosis

- Conditional recommendation.
- Evidence level: C.
- Voting: 67 votes, median vote rating 8 (IQR 7–9).

Fig. 1 | Risk stratification and frequency of screening for IIM-related cancer. The recommendations apply only to adult patients diagnosed with idiopathic inflammatory myopathy (IIM) within the 3-year period after IIM symptom onset. Individual patients with adult-onset IIM can be risk-stratified according to IIM subtype, myositis-specific antibody (MSA) and myositis-associated autoantibody (MAA) profile and clinical features, resulting in assignment to categories of 'high', 'moderate' or 'standard' risk of IIM-associated cancer. Screening modalities and frequency are recommended according to the assigned risk category. 'Basic' and 'enhanced' screening panels are outlined in the figure. Additional screening with ^{18}F-fluoro-deoxy-glucose PET–CT (^{18}F-FDG PET–CT) should be considered for patients with adult-onset IIM who are considered at a 'high risk of IIM-related cancer' where underlying cancer has not been detected by investigations at the time of IIM diagnosis or as a single screening investigation for patients with anti-TIF1γ antibody-positive dermatomyositis with disease onset at age >40 years and with ≥1 additional 'high risk' clinical feature. Clinicians should consider carrying out upper and lower gastrointestinal endoscopy for patients with adult-onset IIM at 'a high risk of IIM-related cancer', where underlying cancer has not been detected by investigations at the time of IIM diagnosis, and nasoendoscopy at the time of diagnosis of adult-onset IIM in geographical regions where the risk of nasopharyngeal carcinoma is increased. Screening for IIM-associated cancer is not routinely required for patients with juvenile-onset IIM or verified inclusion body myositis. ASSD, anti-synthetase syndrome; CADM, clinically amyopathic dermatomyositis; HMGCR, 3-hydroxy 3-methylutaryl coenzyme A reductase; IBM, inclusion body myositis; IMNM, immune-mediated necrotizing myopathy; MDA5, melanoma differentiation-associated gene 5; NXP2, nuclear matrix protein 2; RNP, ribonucleoprotein; SAE1, small ubiquitin-like modifier-1 activating enzyme; SRP, signal recognition particle; TIF1γ, transcription intermediary factor 1γ. [a]Anti-PM-Scl, anti-Ku, anti-RNP, anti-SSA/Ro, anti-SSB/La antibodies. [b]If not already part of country/region-specific age- and sex-appropriate cancer screening programmes. Adapted with permission from[41].

Recommendation 15. Clinicians should consider carrying out an ^{18}F-FDG PET–CT scan as a single screening investigation for patients with anti-TIF1γ antibody-positive dermatomyositis with disease onset at age >40 years and with ≥1 additional 'high risk' clinical feature

- Conditional recommendation.
- Evidence level: C.
- Voting: 67 votes, median vote rating 8 (IQR 7–9).

A growing body of evidence demonstrates the utility of ^{18}F-FDG PET–CT as a screening modality for IIM-associated cancer[33–37]. The Expert Group deemed it appropriate to form a conditional recommendation relating to the use of ^{18}F-FDG PET–CT scanning as a screening method only in those with a 'high' risk of cancer when 'basic' and 'enhanced' screening panels have not identified a cancer, especially if lymphoma is suspected. Evidence has also shown that ^{18}F-FDG PET–CT can identify cancers at a comparable rate with a large number of conventional screening investigations, including complete physical examination, laboratory tests (complete blood count and serum chemistry panel), thoraco-abdominal CT scan, tumour markers (CA125, CA19-9, CEA and PSA), gynaecological examination, ovarian ultrasonography and mammography[34]. The Expert Group therefore agreed that ^{18}F-FDG PET–CT could be considered as a single screening method in patients with dermatomyositis with onset at age >40 years with anti-TIF1γ antibody positivity and ≥ 1 additional 'high risk' clinical feature, thus potentially facilitating an earlier diagnosis and the need for fewer investigations. Clinicians should, however, balance the increased cancer risk attributed to ^{18}F-FDG PET–CT-related radiation exposure against the benefit of potential cancer detection. The Expert Group also acknowledged that ^{18}F-FDG PET–CT might not be available in all health care systems.

Recommendation 16. Clinicians should consider carrying out upper and lower gastrointestinal endoscopy for patients with adult-onset IIM at a 'high risk of IIM-related cancer', where underlying cancer has not been detected by investigations at the time of IIM diagnosis

- Conditional recommendation.
- Evidence level: D.
- Voting: 67 votes, median vote rating 8 (IQR 7–9).

The gastrointestinal tract is a common site of cancer in people with IIM-associated cancer[5]. Evidence relating to the utility of upper and lower gastrointestinal endoscopy as a cancer screening modality in patients with IIM is limited and this procedure confers potential risks (for example, bowel perforation)[33,38,39]; therefore, the Expert Group formed a conditional recommendation. Upper and lower gastrointestinal endoscopy should be considered after other cancer screening investigations, including 'basic' and 'enhanced' screening panels, have been carried out in patients with adult-onset IIM at a high risk of IIM-related cancer. The Expert Group recognized that upper and/or lower gastrointestinal endoscopy could be carried out as part of country- or region-specific age- and sex-appropriate cancer screening programmes.

Recommendation 17. Clinicians should consider carrying out nasoendoscopy at the time of diagnosis in patients with adult-onset IIM in geographical regions where the risk of nasopharyngeal carcinoma is increased

- Conditional recommendation.
- Evidence level: D.
- Voting: 67 votes, median vote rating 8 (IQR 7–9).

The nasopharynx is a leading site of IIM-associated cancer in certain populations, especially those of East Asian and South-East Asian heritage; a 2021 meta-analysis estimated a prevalence of nasopharyngeal cancer in adults with dermatomyositis of 37% in Hong Kong, 28% in Malaysia and 12% in Singapore[40]. Consideration of nasoendoscopy is therefore advocated as a cancer screening modality for patients at a high risk of nasopharyngeal cancer.

Recommendation 18. Clinicians should consider cancer screening in all patients with IIM with the following 'red-flag' symptoms or clinical features, regardless of risk category: unintentional weight loss, family history of cancer, smoking, unexplained fever or night sweats

- Conditional recommendation.
- Evidence level: D.
- Voting: 66 votes, median vote rating 9 (IQR 7–9).

The Expert Group recognized that identification of certain 'red flag' symptoms or clinical features can aid clinicians in identifying patients with underlying IIM-associated cancer. Clinicians should identify organ-specific features of cancer during the comprehensive history and examination (recommendation 9), such as haemoptysis (potentially a symptom of lung cancer) and dysphagia (potentially a symptom of oesophageal cancer).

Discussion

The International Guideline for IIM-Associated Cancer Screening provides, for the first time, evidence-supported and consensus-based recommendations addressing IIM-associated cancer risk stratification for the individual patient, cancer screening modalities and screening frequency.

The recommendations provide practical guidance for clinicians serving IIM populations across varying countries and health systems. Implementation of the recommendations is aimed at facilitating early detection of IIM-associated cancer, especially in those at a high risk, thus potentially improving outcomes, including survival. The recommendations can help to standardize cancer screening practices for use in patients with IIM across the globe, especially benefitting those without access to specialist services. Recommendations can foster open and clear clinician–patient discussions regarding individualized cancer risk and facilitate shared decision-making.

This guideline has a number of strengths. First, the recommendations were developed via a process that assimilated current evidence, the results of a meta-analysis, and experts' experience and expertise, thus maximizing the applicability of the recommendations to clinical care. Second, the recommendations were formed by a large (n = 75) Expert Group with academic expertise in IIM management (in rheumatology, neurology, respiratory medicine and dermatology) and cancer screening. Members of the Expert Group were located in a wide variety of countries with varying health systems and populations, thus ensuring international applicability of the recommendations. Third, formation of the recommendations via an online questionnaire using the Delphi process conferred a number of benefits: assurance of anonymity, thus reducing peer influence; equal weighting of each response; and practicality of response collation, thus facilitating involvement of international Expert Group members without the need for a face-to-face meeting. Finally, input from three patient partners allowed for assessment of the guidelines from a practical perspective, with the added benefit of improving engagement and integration into clinical systems.

This guideline nonetheless has a number of limitations. First, the evidence base pertaining to the utility of IIM-associated cancer screening approaches is markedly limited, thus reducing the strength of the recommendations. Indeed, no recommendation had a 'high (A)' quality body of supporting evidence, thus highlighting the pressing need for high-quality studies that can strengthen the evidence base and inform future iterations of this guideline. Second, although the Expert Group comprised members from 22 countries, geographic diversity was limited, with representation from a restricted number of countries or regions (27 members were from the USA, 30 were from Europe). Specifically, no Expert Group member practised in any country from Africa, only one member was from China, one was from South America and no members were from Indonesia or Pakistan, which have the fourth and fifth largest populations in the world. This disparity illustrates the international distribution of IIM specialists and future iterations of this guideline should ensure wider inclusion, where possible. Indeed, implementation of recommendations might not be possible in all countries and health systems, especially in resource-challenged areas; future iterations of the guideline should aim to address identified disparities. Finally, the definition of cancer risk groups was based on available evidence, not empirical research. Future research focusing upon the ability of the risk stratification groups to accurately differentiate and predict cancer development is warranted and will influence subsequent iterations of this guideline.

The guideline development process has highlighted a number of unmet needs, thus facilitating the formation of a research agenda. First, the utility of the cancer screening recommendations have not been empirically investigated; research addressing this topic could guide future iterations and improve clinicians' ability to detect cancer. Second, no study investigated the utility of repeated screening or determined optimal screening frequency; research specifically addressing the optimal frequency and/or interval of screening, especially CT scanning of the thorax, abdomen and pelvis, could greatly enhance cancer detection. Third, future research investigating complications or harm resulting from this guideline's recommendations is vital; for example, identification of the number of false-positive cancer diagnoses and any resulting harm via recommended screening will be key in the formation of future iterations of the guideline.

It is anticipated that revision of this guideline after a 5-year period will be appropriate, thus allowing for the inclusion of emerging research and findings into the evidence base upon which recommendations can be revised and created.

An audit tool, developed by the Steering Committee, is included (see Supplementary Table 10) to enable clinicians and clinical teams to measure their concordance with recommendations, thus aiding service quality improvement.

Conclusions

In conclusion, this International Guideline for IIM-Associated Cancer Screening provides guidance to clinicians and patients regarding individual-patient risk stratification, cancer screening modalities and screening frequency. The guideline standardizes patient care and provides a foundation upon which future IIM-cancer screening research can build.

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References

1. Oldroyd, A., Lilleker, J. & Chinoy, H. Idiopathic inflammatory myopathies — a guide to subtypes, diagnostic approach and treatment. *Clin. Med.* **17**, 322–328 (2017).
2. Chinoy, H. & Cooper, R. G. In *Oxford Textbook of Rheumatology* (eds Watts, R. A. et al.) 1009–1020 (Oxford Univ. Press, 2013).
3. Qiang, J. K., Kim, W. B., Baibergenova, A. & Alhusayen, R. Risk of malignancy in dermatomyositis and polymyositis: a systematic review and meta-analysis. *J. Cutan. Med. Surg.* **21**, 131–136 (2017).
4. Dobloug, G. C., Garen, T., Brunborg, C., Gran, J. T. & Molberg, Ø. Survival and cancer risk in an unselected and complete Norwegian idiopathic inflammatory myopathy cohort. *Semin. Arthritis Rheum.* **45**, 301–308 (2015).
5. Kang, E. H. et al. Temporal relationship between cancer and myositis identifies two distinctive subgroups of cancers: impact on cancer risk and survival in patients with myositis. *Rheumatology* **55**, 1631–1641 (2016).
6. Hočevar, A. et al. Survival of patients with idiopathic inflammatory myopathies in Slovenia. *Front. Med.* **8**, 801078 (2021).
7. Dobloug, G. C., Svensson, J., Lundberg, I. E. & Holmqvist, M. Mortality in idiopathic inflammatory myopathy: results from a Swedish nationwide population-based cohort study. *Ann. Rheum. Dis.* **77**, 40–47 (2018).
8. Nuño-Nuño, L. et al. Mortality and prognostic factors in idiopathic inflammatory myositis: a retrospective analysis of a large multicenter cohort of Spain. *Rheumatol. Int.* **37**, 1853–1861 (2017).
9. Oldroyd, A. G. S. et al. A systematic review and meta-analysis to inform cancer screening guidelines in idiopathic inflammatory myopathies. *Rheumatology* **60**, 2615–2628 (2021).
10. Moher, D., Liberati, A., Tetzlaff, J. & Altman, D. G. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* **6**, e1000097 (2009).
11. Scottish Intercollegiate Guidelines Network. *SIGN 50: a Guideline Developer's Handbook* (2019).
12. Gunawardena, H. et al. Clinical associations of autoantibodies to a p155/140 kDa doublet protein in juvenile dermatomyositis. *Rheumatology* **47**, 324–328 (2007).
13. Sato, J. D. O. et al. A Brazilian registry of juvenile dermatomyositis: onset features and classification of 189 cases. *Clin. Exp. Rheumatol.* **27**, 1031–1038 (2009).
14. Na, S. J., Kim, S. M., Sunwoo, I. N. & Choi, Y. C. Clinical characteristics and outcomes of juvenile and adult dermatomyositis. *J. Korean Med. Sci.* **24**, 715–721 (2009).

15. Dawkins, M. A. et al. Dermatomyositis: a dermatology-based case series. *J. Am. Acad. Dermatol.* **38**, 397–404 (1998).
16. Sun, C. et al. Juvenile dermatomyositis: a 20-year retrospective analysis of treatment and clinical outcomes. *Pediatr. Neonatol.* **56**, 31–39 (2015).
17. Ponyi, A. et al. Cancer-associated myositis: clinical features and prognostic signs. *Ann. N. Y. Acad. Sci.* **1051**, 64–71 (2005).
18. Morris, P. & Dare, J. Juvenile dermatomyositis as a paraneoplastic phenomenon: an update. *J. Pediatr. Hematol. Oncol.* **32**, 189–191 (2010).
19. Limaye, V. et al. The incidence and associations of malignancy in a large cohort of patients with biopsy-determined idiopathic inflammatory myositis. *Rheumatol. Int.* **33**, 965–971 (2013).
20. Greenberg, S. A., Pinkus, J. L., Amato, A. A., Kristensen, T. & Dorfman, D. M. Association of inclusion body myositis with T cell large granular lymphocytic leukaemia. *Brain* **139**, 1348–1360 (2016).
21. Greenberg, S. A. et al. Highly differentiated cytotoxic T cells in inclusion body myositis. *Brain* **142**, 2590–2604 (2019).
22. Ebell, M. H., Thai, T. N. & Royalty, K. J. Cancer screening recommendations: an international comparison of high income countries. *Public. Health Rev.* **39**, 7 (2018).
23. Yang, H. et al. Identification of multiple cancer-associated myositis-specific autoantibodies in idiopathic inflammatory myopathies: a large longitudinal cohort study. *Arthritis Res. Ther.* **19**, 259 (2017).
24. Ichimura, Y. et al. Anti-nuclear matrix protein 2 antibody-positive inflammatory myopathies represent extensive myositis without dermatomyositis-specific rash. *Rheumatology* **61**, 1222–1227 (2022).
25. Fujimoto, M. et al. Myositis-specific anti-155/140 autoantibodies target transcription intermediary factor 1 family proteins. *Arthritis Rheum.* **64**, 513–522 (2012).
26. Oldroyd, A. et al. The temporal relationship between cancer and adult onset anti-transcriptional intermediary factor 1 antibody-positive dermatomyositis. *Rheumatology* **58**, 650–655 (2019).
27. Targoff, I. N. et al. A novel autoantibody to a 155-kd protein is associated with dermatomyositis. *Arthritis Rheum.* **54**, 3682–3689 (2006).
28. Ikeda, N. et al. Clinical significance of serum levels of anti-transcriptional intermediary factor 1-γ antibody in patients with dermatomyositis. *J. Dermatol.* **47**, 490–496 (2020).
29. Ly, N. T. M. et al. Clinical and laboratory parameters predicting cancer in dermatomyositis patients with anti-TIF1γ antibodies. *J. Dermatol. Sci.* **104**, 177–184 (2021).
30. Loarce-Martos, J., Lilleker, J. B., Parker, M., McHugh, N. & Chinoy, H. Polymyositis: is there anything left? A retrospective diagnostic review from a tertiary myositis centre. *Rheumatology* **60**, 3398–3403 (2020).
31. Mariampillai, K. et al. Development of a new classification system for idiopathic inflammatory myopathies based on clinical manifestations and myositis-specific autoantibodies. *JAMA Neurol.* **75**, 1528–1537 (2018).
32. Allenbach, Y. et al. High risk of cancer in autoimmune necrotizing myopathies: usefulness of myositis specific antibody. *Brain* **139**, 2131–2135 (2016).
33. Maliha, P. G., Hudson, M., Abikhzer, G., Singerman, J. & Probst, S. ^{18}F-FDG PET/CT versus conventional investigations for cancer screening in autoimmune inflammatory myopathy in the era of novel myopathy classifications. *Nucl. Med. Commun.* **40**, 377–382 (2019).
34. Selva-O'Callaghan, A. et al. Conventional cancer screening versus PET/CT in dermatomyositis/polymyositis. *Am. J. Med.* **123**, 558–562 (2010).
35. Trallero-Araguás, E. et al. Cancer screening in idiopathic inflammatory myopathies: ten years experience from a single center. *Semin. Arthritis Rheum.* **53**, 151940 (2022).
36. Li, Y., Zhou, Y. & Wang, Q. Multiple values of ^{18}F-FDG PET/CT in idiopathic inflammatory myopathy. *Clin. Rheumatol.* **36**, 2297–2305 (2017).
37. Bradhurst, P., Limaye, S. & Kane, B. Review of cancer screening investigations in new diagnoses of idiopathic inflammatory myopathies at a single tertiary hospital. *J. Clin. Rheumatol.* **28**, E274–E277 (2022).
38. Leatham, H. et al. Evidence supports blind screening for internal malignancy in dermatomyositis: data from 2 large US dermatology cohorts. *Medicine* **97**, e9639 (2018).
39. Sparsa, A. et al. Routine vs extensive malignancy search for adult dermatomyositis and polymyositis: a study of 40 patients. *Arch. Dermatol.* **138**, 885–890 (2002).
40. Irekeola, A. A. et al. Prevalence of nasopharyngeal carcinoma in patients with dermatomyositis: a systematic review and meta-analysis. *Cancers* **13**, 1886 (2021).
41. Oldroyd, A. et al. Cancer Screening Recommendations for Patients with Idiopathic Inflammatory Myopathy [abstract]. *Arthritis Rheumatol.* **74** (suppl. 9). https://acrabstracts.org/abstract/cancer-screening-recommendations-for-patients-with-idiopathic-inflammatory-myopathy/ (2022).

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Author contributions

All authors made a substantial contribution to discussion of the content, wrote the article and reviewed and/or edited the manuscript before submission.

Competing interests

R.A. served as a consultant for Kezar, Csl Behring, AstraZeneca, Octapharma, BMS, Pfizer, Janssen, Mallinckrodt, Alexion, Q32, argenx, Boehringer-Ingelheim, Corbus and EMD-Serono, and received research funding from Pfizer, BMS, Genentech, Kezar, Csl Behring and Mallinckrodt; L.C. has received funding from Boerhinger Ingelheim, served on an advisory board for Eicos Sciences and Mitsubishi Tanabe, and has received consulting fees from Kyverna, Jasper and Genentech; P.M.M. has received consulting/speaker's fees from AbbVie, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB, outside the submitted work; R.A.V. has received a research grant from Pfizer; H.C. has received research grants, travel grants, consultancy or speaker honoraria from AbbVie, Amgen, BMS, Biogen, Janssen, Lilly, Novartis and UCB; V.P.W. served as a consultant for Kezar, CSL Behring, AstraZeneca, Octapharma, Pfizer, Janssen, Neovacs and Idera, and has received research funding from Pfizer, CSL Behring and Corbus; L.A.O. has received consulting/speaker's fees from AbbVie, BMS, Boehringer Ingelheim, Eli Lilly, Janssen, Novartis, Pfizer and Roche, outside the submitted work; J.P.C. owns stock in trust accounts in the following companies: AbbVie, Abbott Laboratories, Amgen, Allergan, Celgene, 3M, Merck, Johnson and Johnson, Procter and Gamble, Pfizer, Gilead, Walgreens and CVS, and has served on a Safety Monitoring committee for Principia Biopharma and as an adjudicator for study entry for EMD Serono and Biogen; C.C.-S. has served as a consultant for AbbVie, Gilead, Octapharma, Pfizer and Regeneron-Sanofi and has received research funding from AbbVie, Bristol-Myers Squibb, Octapharma and Pfizer; B.F.C. has served as a consultant for Biogen Inc., Bristol Meyers Squibb, Horizon Therapeutics and EMD Serono, has received research funding from Daavlin Company, and is an investigator for Pfizer Inc and Biogen Inc; P.F.D. works for UpToDate, serves on an FDA Advisory committee, has received research grants in the past 3 years from Genentech and Bristol Myers, and was on an unpaid advisory group for Boehringer Ingelheim; L.P.D. has received speaker honoraria from Boehringer Ingelheim and has served on a data safety monitoring board for Corbus Pharmaceuticals; M.M.D. serves or has recently served as a consultant for Abcuro, Amazentis, argenx, Catalyst, Cello, Covance/Labcorp, CSL-Behring, EcoR1, Janssen, Kezar, MDA, Medlink, Momenta, NuFactor, Octapharma, Priovant, RaPharma/UCB, Roivant Sciences Inc, Sanofi Genzyme, Shire Takeda, Scholar Rock, Spark Therapeutics, Abata/Third Rock, UCB Biopharma and UpToDate, and has received research grants or contracts or educational grants from Alexion, Alnylam Pharmaceuticals, Amicus, Biomarin, Bristol-Myers Squibb, Catalyst, Corbus, CSL-Behring, FDA/OOPD, GlaxoSmithKline, Genentech, Grifols, Kezar, Mitsubishi Tanabe Pharma, MDA, NIH, Novartis, Octapharma, Orphazyme, Ra Pharma/UCB, Sanofi Genzyme, Sarepta Therapeutics, Shire Takeda, Spark Therapeutics, The Myositis Association, UCB Biopharma/RaPharma and Viromed/Healixmith; F.E. has received research support and funding from Genentech and Octapharma; D.F. has received honoraria from Bristol-Meyers Squibb, Kyverna, Janssen, Amgen, UCB, Priovant and Merck, funding for contracted research from Pfizer and a research grant from Serono; Z.G. has received speaker honoraria from AbbVie, Eli Lilly, Novartis and Roche, and has served on an advisory board for Octapharma. A.J.vdK. has served on an advisory board for argenx; M.K. has received research grants, travel grants, consultancy or speaker honoraria from AbbVie, argenx, Astellas, Boehringer Ingelheim, Chugai, Corbus, Horizon Therapeutics, Kissei, Medical & Biological Laboratories, Mochida, Ono and Mitsubishi Tanabe; I.E.L. has received consulting fees from Corbus Pharmaceuticals Inc and research grants from Astra Zeneca, has served on the advisory board for Bristol-Myers Squibb, Corbus Pharmaceutical, EMD Serono Research & Development Institute, argenx, Octapharma, Kezaar, Orphazyme, Pfizer and Janssen, and has stock shares in Roche and Novartis; C.A.M. has served a consultant for Boerhinger Ingelheim and for the National Vaccine Injury Compensation Program; J.J.P. has received consultant fees from Alexion, Riovant, argenx, EMD-Serono, Pfizer, Kezar and Guidepoint, and clinical trial research support from Alexion, Pfizer and Kezar; J.R. has received departmental research support from the Dutch Prinses Beatrix Spierfonds, Dutch ALS foundation, Marigold foundation, Prothya Biosolutions, argenx and Health-Holland/Dutch Ministry of Economic Affairs; L.G.R. has served as an unpaid consultant for AstraZeneca, CSL Behring, Alexion, Boehringer Ingelheim, Argenx, Pfizer and Horizon Therapeutics, and has received research

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Additional information

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