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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

In the format provided by the authors and unedited

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

A. Composition of the Expert Group
B. Results of Delphi surveys
C. Recommendations and corresponding evidence
D. International Guideline for IIM-Associated Cancer Screening Audit tool

A. Composition of the Expert Group

Supplementary Table 1. Composition of the Expert Group by specialty and location

Speciality	Total	By continent				
		North America	South America	Europe	Asia	Australia
Rheumatology	46	22	1	18	4	1
Neurology	12	4	0	5	1	2
Dermatology	9	7	0	0	2	0
Oncology	3	0	0	3	0	0
Pulmonary	2	1	0	1	0	0
Cancer screening expert	2	0	0	2	0	0
Paediatric rheumatology	1	1	0	0	0	0
Total	75	35	1	29	7	3

B. Results of Delphi surveys

Round 1 - collation of Expert Group opinion regarding IIM-associated cancer risk factors

Supplementary Table 2: "Do you think X is a risk factor, protective factor or neutral factor for cancer in people presenting with new onset IIM?"

Factor	Risk	Neutral	Protective	Consensus	Responses
	%	%	%		
Increased age	99	1	0	Risk	68
Male sex	67	33	0	Risk	67
Female sex	7	84	9	Neutral	69
Dysphagia	68	30	1	Risk	69
Cutaneous necrosis/ulceration	68	26	6	Risk	69
Raynaud's	0	35	65	Protective	69
ILD	6	20	74	Protective	69
Fever	4	81	14	Neutral	69
Inflamm arthritis	1	57	41	Neutral	68
Mechanic's hands	3	53	44	Neutral	68
Sicca	3	80	17	Neutral	69
Telangiectasia	9	79	12	Neutral	68
Sclerodactyly	3	70	28	Neutral	69
DM	99	1	0	Risk	69
PM	46	35	19	Risk	69
ASSD	12	37	51	Protective	67
CADM	49	28	23	Risk	69
IMNM	28	61	10	Neutral	67
IBM	9	72	19	Neutral	67
Juvenile IIM	10	58	32	Neutral	69
TIF1	100	0	0	Risk	69
NXP2	65	35	0	Risk	69
SAE1	26	68	6	Neutral	69
HMGCR	15	65	21	Neutral	68
MDA5	10	52	38	Neutral	69
Mi2	13	65	22	Neutral	69
SRP	3	69	28	Neutral	68
Jo1	0	26	74	Protective	68
Non-Jo1 ASSD ab	1	36	62	Protective	69
MSA negativity	30	67	3	Neutral	69
PmScl	3	78	19	Neutral	69
Ku	0	87	13	Neutral	67
U1RNP	0	80	20	Neutral	69
U2RNP	0	90	10	Neutral	67
U3RNP	0	88	12	Neutral	67
Ro52	1	79	19	Neutral	68
Ro60	1	87	12	Neutral	68

ASSD = anti-synthetase syndrome; CADM = clinically amyopathic dermatomyositis; DM = dermatomyositis; HMGCR = 3-hydroxy 3-methylutaryl coenzyme A reductase; IBM = inclusion body myositis; IIM = idiopathic inflammatory myopathy; ILD = interstitial lung disease; IMNM = immune-mediated necrotising myopathy; MDA5 = melanoma differentiation-associated gene 5; MSA = myositis specific autoantibody; NXP2 = nuclear matrix protein 2; PM = polymyositis; RNP = ribonucleoprotein SAE1 = small ubiquitin-like modifier-1 activating enzyme; SRP = signal recognition particle; TIF1-gamma = transcriptional intermediary factor 1

Supplementary Table 3: “Do you think that all people with new onset IIM should undergo X, with the aim of identifying symptoms of underlying cancer?”

Screening modality	Yes	No	Consensus	Responses
	%	%		
History	94	6	Yes	69
Physical examination	93	7	Yes	68
CBC	90	10	Yes	69
LFTs	78	22	Yes	69
Urinalysis	65	35	Yes	68
ESR	57	43	Yes	68
CRP	58	42	Yes	69

CBC = complete blood count; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; IIM = idiopathic inflammatory myopathy; LFT = liver function test

Supplementary Table 4: “Do you think X should be carried out in all IIM patients, only those with cancer risk factors, or none?”

Screening modality	All	Only those with RFs	None	Consensus	Responses
	%	%	%		
CXR	62	17	20	All	69
CT neck, chest, abdomen, and pelvis	41	58	1	With RFs	69
Ovarian USS	35	62	3	With RFs	69
Testicular USS	17	61	22	With RFs	69
^{18}F-FDG PET/CT	3	72	25	With RFs	69
Mammography	57	41	3	All	69
Whole body MRI	4	26	70	None	69
PSA	46	54	0	With RFs	68
CA-125	25	45	30	With RFs	69
CA15-3	14	41	45	None	69
CA19-9	18	44	38	With RFs	68
Alpha-fetoprotein	13	33	54	None	69
Gastroscopy	10	74	16	With RFs	69
Colonoscopy	17	75	7	With RFs	69
Naso-endoscopy	0	56	44	With RFs	68
Cervical smear	57	39	4	All	69

CT = computed tomography; CXR = chest X-ray radiograph; ^{18}F-FDG PET/CT = [18F]-fluoro-deoxy-glucose positron emission tomography/computed tomography; IIM, idiopathic inflammatory myopathy; MRI = magnetic resonance imaging; PSA = prostate specific antigen; RF, risk factor; USS = ultrasound scan

Round 2 - voting on draft recommendations

Supplementary Table 5: Round 2 voting on draft recommendations

Number	Recommendation	Consensus		
		No. responses	Median score (IQR)	Outcome
1	Underlying cancer risk of adult IIM patients should be stratified according to subtype in the following manner: High risk - a. Dermatomyositis Intermediate risk - a. Clinically amyopathic dermatomyositis b. Polymyositis Low risk - a. Anti-synthetase syndrome b. Immune-mediated necrotising myopathy c. Connective tissue disease-overlap	64	7 (6, 8)	Agreement
2	Cancer screening is not routinely required in patients with juvenile-onset IIM	62	8 (8,9)	Agreement
3	Cancer screening is not routinely required in patients with verified inclusion body myositis	62	8 (7, 9)	Agreement
4	Underlying cancer risk of adult IIM patient should be stratified according to autoantibody status in the following manner: High risk - a. Anti-TIF1-gamma positivity b. Anti-NXP2 positivity Intermediate risk - a. Anti-SAE1 positivity b. Anti-HMGCR positivity c. Anti-MDA5 positivity d. Anti-Mi2 positivity e. Anti-SRP positivity f. Myositis-specific autoantibody negativity Low risk - a. Anti-Jo1 positivity b. Non-Jo1 ASSD antibody positivity c. Myositis-associated antibody positivity (PM-Scl, Ku, RNP, Ro/La [SSA/B])	64	7 (6, 8)	Agreement
5	All adult patients with new onset IIM should be tested for myositis-specific autoantibodies and myositis-associated autoantibodies to assist stratification of cancer risk.	64	9 (8, 9)	Agreement
6	Underlying cancer risk of adult IIM patients should be stratified according to clinical features in the following manner: High risk - a. Age >45 years at the time of onset b. Male gender c. Dysphagia d. Cutaneous necrosis/ulceration e. Persistent high disease activity despite immunosuppressive therapy	64	8 (6, 9)	Agreement

	Low risk - a. Raynaud's b. Inflammatory arthropathy c. Interstitial lung disease			
7	All adult IIM patients should continue to participate in country/region-specific age and sex appropriate cancer screening programmes.	64	9 (9, 9)	Agreement

ASSD = anti-synthetase syndrome; HMGCR = 3-hydroxy 3-methylutaryl coenzyme A reductase; IIM = idiopathic inflammatory myopathy
IQR = interquartile range; 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; TIF1-gamma = transcriptional intermediary factor 1

Round 3 - voting on draft recommendations

Supplementary Table 6: Round 3 voting on draft recommendations

Number	Recommendation	Consensus		
		No. responses	Median score (IQR)	Outcome
1	Underlying cancer risk of adult IIM patients should be stratified according to subtype in the following manner: High risk - a. Dermatomyositis Intermediate risk - a. Clinically amyopathic dermatomyositis b. Polymyositis c. Immune-mediated necrotising myopathy Low risk - a. Anti-synthetase syndrome b. Overlap myositis/connective tissue disease-associated myositis	52	8 (7, 9)	Agreement
4	Underlying cancer risk of adult IIM patient should be stratified according to autoantibody status in the following manner: High risk - a. Anti-TIF1-gamma positivity b. Anti-NXP2 positivity Intermediate risk - a. Anti-SAE1 positivity b. Anti-HMGCR positivity c. Anti-Mi2 positivity d. Anti-MDA5 positivity Low risk - a. Anti-SRP positivity b. Anti-Jo1 positivity c. Non-Jo1 ASSD antibody positivity d. Myositis-associated antibody positivity (PM-Scl, Ku, RNP, Ro/La [SSA/B])	52	8 (7, 8)	Agreement
8	Adult IIM patients that fulfil any of the following criteria should be considered to have a “high risk for IIM-related cancer”: • High risk autoantibody • DM • ≥ 2 high risk clinical features (dysphagia, cutaneous necrosis/ulceration, persistent high disease activity despite immunosuppressive therapy)	51	8 (7, 9)	Agreement
9	Adult IIM patients that fulfil any of the following criteria should be considered to have an “intermediate risk for IIM-related cancer”, unless high risk criteria fulfilled: • Intermediate risk autoantibody • PM • Seronegative IMNM • CADM • Male aged >45 years	51	7 (7, 8)	Agreement

10	Adult IIM patients that fulfil any of the following criteria should be considered to have a "low risk for IIM-related cancer", unless intermediate or high-risk criteria fulfilled: • Low risk autoantibody • ASSD • Seropositive IMNM • CTD-overlap • Absent high risk clinical features • ≥ 1 low risk clinical features	51	8 (7, 9)	Agreement
11	"Basic cancer screening" should include the following investigations (in addition to country/region-specific age and sex appropriate cancer screening programmes for the general population): a. Comprehensive history b. Comprehensive physical examination c. Complete blood count d. Serum liver function tests e. Serum erythrocyte sedimentation rate/plasma viscosity f. Serum C-reactive protein g. Serum protein electrophoresis h. Urinalysis i. Plain chest X-ray radiograph	50	7 (6, 8)	Agreement
12	"Enhanced cancer screening" should include the following investigations: a. CT scan of the neck, thorax, abdomen, and pelvis b. Cervical screening (i.e. smear test)* c. Mammography* d. Prostate-specific antigen* e. CA-125 f. Pelvic/trans-vaginal USS for ovarian cancer g. Faecal occult blood* *If not already part of country/region-specific age and sex appropriate screening programmes.	51	8 (7, 8)	Agreement

ASSD = anti-synthetase syndrome; CADM = clinically amyopathic dermatomyositis; CT = computed tomography; CTD = connective tissue disease; DM = dermatomyositis; HMGCR = 3-hydroxy 3-methylutaryl coenzyme A reductase; IIM = idiopathic inflammatory myopathy; IMNM = immune-mediated necrotising myopathy; IQR = interquartile range; MDA5 = melanoma differentiation-associated gene 5; NXP2 = nuclear matrix protein 2; PM = polymyositis; RNP = ribonucleoprotein; SAE1 = small ubiquitin-like modifier-1 activating enzyme; SRP = signal recognition particle; TIF1-gamma = transcriptional intermediary factor 1; USS = ultrasound scan

Round 4 - voting on draft recommendations

Supplementary Table 7: Round 4 voting on draft recommendations

Number	Recommendation	Consensus		
		No. responses	Median score (IQR)	Outcome
1, 4, 6 combined	Underlying cancer risk of adult IIM patients should be stratified according to subtype, autoantibody status, and clinical features in the following manner: High risk - a. Dermatomyositis b. Anti-TIF1-gamma positivity c. Anti-NXP2 positivity d. Age >40 years at the time of onset e. Features of persistent high disease activity despite immunosuppressive therapy (including relapse of previously controlled disease) f. Dysphagia (moderate to severe) g. Cutaneous necrosis/ulceration Intermediate risk - a. Clinically amyopathic dermatomyositis b. Polymyositis c. Immune-mediated necrotising myopathy d. Anti-SAE1 positivity e. Anti-HMGCR positivity f. Anti-Mi2 positivity g. Anti-MDA5 positivity h. Male sex Low risk - a. Anti-synthetase syndrome b. Overlap IIM/connective tissue disease-associated myositis c. Anti-SRP positivity d. Anti-Jo1 positivity e. Non-Jo1 ASS antibody positivity f. Myositis-associated antibody positivity (PM-Scl, Ku, RNP, Ro/La [SSA/B]) g. Raynaud's h. Inflammatory arthropathy i. Interstitial lung disease	52	8 (7, 9)	Agreement
8	Adult IIM patients with two or more "high risk" factors (subtype, autoantibody, or clinical feature) should be considered to have a "high risk for IIM-related cancer".	67	8 (8, 9)	Agreement
9	Adult IIM patients with 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 have an "intermediate risk for IIM-related cancer".	67	7 (7, 9)	Agreement
10	Adult IIM patients that do not fulfil the "high" or "intermediate risk" definitions should be considered to have "low risk for IIM-related cancer".	67	8 (7, 9)	Agreement

11	"Basic cancer screening" should include the following investigations (in addition to country/region-specific age and sex appropriate cancer screening programmes for the general population): a. Comprehensive history b. Comprehensive physical examination c. Complete blood count d. Serum liver function tests e. Serum erythrocyte sedimentation rate/plasma viscosity f. Serum C-reactive protein g. Serum protein electrophoresis h. Urinalysis i. Plain chest X-ray radiograph	50	7 (6, 8)	Agreement
12	"Enhanced cancer screening" should include the following investigations: a. CT scan of the neck, thorax, abdomen, and pelvis b. Cervical screening (i.e. smear test)* c. Mammography* d. Prostate-specific antigen* e. CA-125 f. Pelvic/trans-vaginal USS for ovarian cancer g. Faecal occult blood* *If not already part of country/region-specific age and sex appropriate screening programmes.	51	8 (7, 8)	Agreement
13	Adult IIM patients at "low risk of IIM-related cancer" should undergo "basic cancer screening" at the time of IIM diagnosis. This is in addition to country/region-specific age and sex appropriate screening programmes for the general population.	67	8 (7, 9)	Agreement
14	Adult IIM patients at "intermediate risk of IIM-related cancer" should undergo "basic screening" and "enhanced screening" at the time of IIM diagnosis.	66	8 (7, 9)	Agreement
15	Adult IIM patients at "high risk of IIM-related cancer" should undergo "enhanced screening" at the time of diagnosis and "basic screening" annually for three years.	67	8 (7, 9)	Agreement
16	Clinicians should consider carrying out an ^{18}F-FDG PET/CT scan for adult IIM patients at "high risk of IIM-related cancer" where underlying cancer has not been detected by investigations at the time of IIM diagnosis.	67	8 (7, 9)	Agreement
17	Clinicians should consider carrying out an ^{18}F-FDG PET/CT scan as a single screening investigation for anti-TIF1-gamma positive DM patients with disease onset >40 years with ≥1 additional high risk clinical feature.	67	8 (7, 9)	Agreement
18	Clinicians should consider carrying out upper and lower gastro-intestinal endoscopy for adult IIM patients at "high risk of IIM-related cancer" where underlying cancer has not been detected by investigations at the time of IIM diagnosis.	67	8 (7, 9)	Agreement
19	Clinicians should consider carrying out naso-endoscopy at the time of diagnosis in adult IIM patients in geographical regions where risk of nasopharyngeal carcinoma is increased.	67	8 (7, 9)	Agreement

20	Clinicians should consider cancer screening in all IIM patients with the following "red-flag" symptoms/clinical features, regardless of risk category: - Unintentional weight loss - Family history of cancer - Smoking - Unexplained fever - Night sweats	66	9 (7, 9)	Agreement

ASSD = anti-synthetase syndrome; CADM = clinically amyopathic dermatomyositis; CT = computed tomography; CTD = connective tissue disease; DM = dermatomyositis; HMGCR = 3-hydroxy 3-methylutaryl coenzyme A reductase; IMNM = immune-mediated necrotising myopathy; IIM = idiopathic inflammatory myopathy; IQR = interquartile range; MDA5 = melanoma differentiation-associated gene 5; NXP2 = nuclear matrix protein 2; PM = polymyositis; RNP = ribonucleoprotein; SAE1 = small ubiquitin-like modifier-1 activating enzyme; SRP = signal recognition particle; TIF1-gamma = transcriptional intermediary factor 1; USS = ultrasound scan; ^{18}F-FDG PET/CT = [18F]-fluoro-deoxy-glucose positron emission tomography/computed tomography

Final recommendations

Note that:

- Recommendations with minor word/phrase changes were presented to the Expert Group for approval prior to manuscript submission
- Recommendation numbering and order was amended for clarity prior to manuscript submission

Supplementary Table 8: Final recommendations

Number	Recommendation	Consensus		
		No. responses	Median score (IQR)	Outcome
1	Screening for IIM-associated cancer is not routinely required in patients with juvenile-onset IIM	62	8 (8, 9)	Agreement
2	Screening for IIM-associated cancer is not routinely required in patients with verified inclusion body myositis	62	8 (7, 9)	Agreement
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.	64	9 (9, 9)	Agreement
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.	64	9 (8, 9)	Agreement
5	Underlying cancer risk of patients with adult-onset IIM should be stratified according to IIM subtype, autoantibody status, and clinical features: High risk - a. DM b. Anti-TIF1-gamma positivity c. Anti-NXP2 positivity d. Age >40 years at the time of onset e. Features of persistent high disease activity despite immunosuppressive therapy (including relapse of previously controlled disease) f. Dysphagia (moderate to severe) g. Cutaneous necrosis/ulceration Intermediate risk - a. CADM b. PM c. IMNM d. Anti-SAE1 positivity e. Anti-HMGCR positivity f. Anti-Mi2 positivity g. Anti-MDA5 positivity h. Male sex Low risk - a. ASSD b. Overlap IIM/connective tissue disease-associated myositis c. Anti-SRP positivity d. Anti-Jo1 positivity e. Non-Jo1 ASSD antibody positivity	52	8 (7, 9)	Agreement

	f. Myositis-associated antibody positivity (PM-Scl, Ku, RNP, Ro/La [SSA/B]) g. Raynaud's phenomenon h. Inflammatory arthropathy i. Interstitial lung disease			
6	Patients with adult-onset IIM who have two or more "high risk" factors (subtype, autoantibody, or clinical feature) should be considered to have "high risk for IIM-related cancer". §	67	8 (8, 9)	Agreement
7	Patients with adult IIM with 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 have "moderate risk for IIM-related cancer". §	67	7 (7, 9)	Agreement
8	Patients with adult-onset IIM that do not fulfil the "high" or "moderate risk" definitions should be considered to have "standard risk for IIM-related cancer". §	67	9 (7, 9)	Agreement
9	"Basic cancer screening" should include the following investigations (in addition to country/region-specific age and gender appropriate cancer screening programmes for the general population): a. Comprehensive history b. Comprehensive physical examination c. Complete blood count d. Serum liver function tests e. Serum erythrocyte sedimentation rate/plasma viscosity f. Serum C-reactive protein g. Serum protein electrophoresis h. Urinalysis i. Plain chest X-ray radiograph	50	7 (6, 8)	Agreement
10	"Enhanced cancer screening" should include the following investigations: a. CT scan of the neck, thorax, abdomen, and pelvis b. Cervical screening (i.e. smear test)* c. Mammography* d. Prostate-specific antigen* e. CA-125 f. Pelvic/trans-vaginal USS for ovarian cancer g. Faecal occult blood* *If not already part of country/region-specific age and sex appropriate screening programmes.	51	8 (7, 8)	Agreement
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.	67	8 (7, 9)	Agreement
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.	66	8 (7, 9)	Agreement
13	Patients with adult-onset IIM at "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 three years.	67	8 (7, 9)	Agreement

14	Clinicians should consider carrying out an ^{18}F-FDG PET–CT scan for patients with adult-onset IIM at 'high risk of IIM-related cancer' where underlying cancer has not been detected by investigations at the time of IIM diagnosis.	67	8 (7, 9)	Agreement
15	Clinicians should consider carrying out an ^{18}F-FDG PET–CT scan as a single screening investigation for patients with anti-TIF1-γ antibody positive dermatomyositis with disease onset at age >40 years and with ≥1 additional 'high risk' clinical feature.	67	8 (7, 9)	Agreement
16	Clinicians should consider carrying out upper and lower gastrointestinal endoscopy for patients with adult-onset IIM at 'high risk of IIM-related cancer' where underlying cancer has not been detected by investigations at the time of IIM diagnosis.	67	8 (7, 9)	Agreement
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.	67	8 (7, 9)	Agreement
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	66	9 (7, 9)	Agreement

ASSD = anti-synthetase syndrome; CADM = clinically amyopathic dermatomyositis; CT = computed tomography; DM = dermatomyositis
HMGCR = 3-hydroxy 3-methylutaryl coenzyme A reductase; IMNM = immune-mediated necrotising myopathy; IIM = idiopathic inflammatory myopathy; IQR = interquartile range; MDA5 = melanoma differentiation-associated gene 5; NXP2 = nuclear matrix protein 2; PM = polymyositis; RNP = ribonucleoprotein; SAE1 = small ubiquitin-like modifier-1 activating enzyme; SRP = signal recognition particle
TIF1-gamma = transcriptional intermediary factor 1; USS = ultrasound scan; ^{18}F-FDG PET/CT = [18F]-fluoro-deoxy-glucose positron emission tomography/computed tomography
§ Risk categories are in comparison to the IIM population, not the general population

C. Supplementary Table 9: Recommendations and corresponding evidence

Number	Recommendation	Corresponding evidence
1	Screening for IIM-associated cancer is not routinely required in patients with juvenile-onset IIM	[1–10]
2	Screening for IIM-associated cancer is not routinely required in patients with verified inclusion body myositis	[11–13]
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.	[14]
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.	[6,14–57]
5	Underlying cancer risk of patients with adult-onset IIM should be stratified according to IIM subtype, autoantibody status, and clinical features: High risk - a. DM b. Anti-TIF1-gamma positivity c. Anti-NXP2 positivity d. Age >40 years at the time of onset e. Features of persistent high disease activity despite immunosuppressive therapy (including relapse of previously controlled disease) f. Dysphagia (moderate to severe) g. Cutaneous necrosis/ulceration Intermediate risk – a. CADM b. PM c. IMNM d. Anti-SAE1 positivity e. Anti-HMGCR positivity f. Anti-Mi2 positivity g. Anti-MDA5 positivity h. Male sex Low risk - a. ASSD b. Overlap IIM/connective tissue disease-associated myositis c. Anti-SRP positivity d. Anti-Jo1 positivity e. Non-Jo1 ASSD antibody positivity f. Myositis-associated antibody positivity (PM-Scl, Ku, RNP, Ro/La [SSA/B]) g. Raynaud's phenomenon h. Inflammatory arthropathy	Dermatomyositis [11,21,24,27,36,44–46,48,49,58–76] Anti-TIF1-gamma positivity [14–24,26–34,36,47,53–57] Anti-NXP2 positivity [14,18,24,27,35–40,47,53] Age >40 years at the time of onset [6,19,26,30,36,45,46,48,65,66,69,71,74,77–90] Persistent high disease activity [30,32,91] Dysphagia [6,31,32,44–46,48–50,56,66,71,78,80,81,92,93] Cutaneous necrosis/ulceration [6,79,81,82,85,87] Clinically amyopathic dermatomyositis [20,65,68,74,75] Polymyositis [11,21,24,27,36,44,46,48,49,58–65,67–73,75,76] Immune-mediated necrotising myopathy [14,27,36,41,42,53,94] Anti-SAE1 positivity [14,27,36,53] Anti-HMGCR positivity [36,41,42,53]

	i. Interstitial lung disease	Anti-Mi2 positivity [14,20,27,36,53,55,57] Anti-MDA5 positivity [14,19,26,27,36,53] Male sex [6,11,19,20,26,30,31,36,44–46,48–50,57–59,64–67,69–71,77–86,92,95,96] Anti-synthetase syndrome [6,14,27,36,43–46,48–53,77] Overlap IIM/connective tissue disease-associated myositis [27,75,89,93] Anti-SRP positivity [14,27,41,53] Anti-Jo1 positivity [6,14,27,36,43–46,48–50,53] Non-Jo1 ASS antibody positivity [14,36,51–53] Myositis-associated antibody positivity (PM-Scl, Ku, RNP, Ro/La [SSA/B]) [27,75,89,93] Raynaud's [14,36,51–53,71,75,87] Inflammatory arthropathy [75,90] Interstitial lung disease [6,11,44–46,48,50,65,66,68,71,75,78,79,89,90,92,93]
6	Patients with adult-onset IIM who have two or more "high risk" factors (subtype, autoantibody, or clinical feature) should be considered to have "high risk for IIM-related cancer". §	As per recommendation 5
7	Patients with adult IIM with 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 have "moderate risk for IIM-related cancer". §	As per recommendation 5
8	Patients with adult-onset IIM that do not fulfil the "high" or "moderate risk" definitions should be considered to have "standard risk for IIM-related cancer". §	As per recommendation 5

9	"Basic cancer screening" should include the following investigations (in addition to country/region-specific age and gender appropriate cancer screening programmes for the general population): a. Comprehensive history b. Comprehensive physical examination c. Complete blood count d. Serum liver function tests e. Serum erythrocyte sedimentation rate/plasma viscosity f. Serum C-reactive protein g. Serum protein electrophoresis h. Urinalysis i. Plain chest X-ray radiograph	Complete blood count [97,98] Comprehensive physical examination [98] Plain chest X-ray radiograph [99]
10	"Enhanced cancer screening" should include the following investigations: a. CT scan of the neck, thorax, abdomen, and pelvis b. Cervical screening (i.e. smear test)* c. Mammography* d. Prostate-specific antigen* e. CA-125 f. Pelvic/trans-vaginal USS for ovarian cancer g. Faecal occult blood* *If not already part of country/region-specific age and sex appropriate screening programmes.	CT scan of the neck, thorax, abdomen, and pelvis [79,97–100] Cervical screening (i.e. smear test) Mammography [97,98] Prostate-specific antigen [97–99] CA-125 [72,89,98–102] Pelvic/trans-vaginal USS for ovarian cancer [98] Faecal occult blood* [99]
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.	NA*
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.	NA*
13	Patients with adult-onset IIM at "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 three years.	NA*
14	Clinicians should consider carrying out an ^{18}F-FDG PET–CT scan for patients with adult-onset IIM at 'high risk of	[98,100,103–106]

	IIM-related cancer' where underlying cancer has not been detected by investigations at the time of IIM diagnosis.	
15	Clinicians should consider carrying out an ^{18}F-FDG PET–CT scan as a single screening investigation for patients with anti-TIF1-γ antibody positive dermatomyositis with disease onset at age >40 years and with ≥1 additional 'high risk' clinical feature.	[98]
16	Clinicians should consider carrying out upper and lower gastrointestinal endoscopy for patients with adult-onset IIM at 'high risk of IIM-related cancer' where underlying cancer has not been detected by investigations at the time of IIM diagnosis.	[79,97,103]
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.	[34,58,107]
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	[79,93,97]

ASSD = anti-synthetase syndrome; CADM = clinically amyopathic dermatomyositis; CT = computed tomography; DM = dermatomyositis; HMGCR = 3-hydroxy 3-methylutaryl coenzyme A reductase; IIM = idiopathic inflammatory myopathy; IMNM = immune-mediated necrotising myopathy; MDA5 = melanoma differentiation-associated gene 5; NXP2 = nuclear matrix protein 2; PM = polymyositis; RNP = ribonucleoprotein; SAE1 = small ubiquitin-like modifier-1 activating enzyme; SRP = signal recognition particle; TIF1-gamma = transcriptional intermediary factor 1; USS = ultrasound scan; ^{18}F-FDG PET/CT = [18F]-fluoro-deoxy-glucose positron emission tomography/computed tomography

* These recommendations had no corresponding evidence base and were formed via expert consensus only

§ Risk categories are in comparison to the IIM population, not the general population

D. Supplementary Table 10: International Guideline for IIM-Associated Cancer Screening Audit tool

Scope:
The purpose of this audit tool is to ensure that the International Guideline for IIM-Associated Cancer Screening is being adhered to. This audit should be undertaken on a sample of adult patients attending secondary or tertiary care.

		YES / NO (✓ or ✗)
1	Is the patient continuing to participate in country/region-specific age and sex appropriate cancer screening programmes?	
2	Has the patient been tested for myositis-specific autoantibodies and myositis-associated autoantibodies?	
3	Has the patient been appropriately risk stratified according to subtype, autoantibody, and clinical features?	
4	Has the patient undergone appropriate screening (i.e. timing of basic and enhanced screening panels) according to their risk category?	
5	If the patient is an adult IIM patient at "high risk of IIM-related cancer" where underlying cancer has not been detected by investigations at the time of IIM diagnosis, have they undergone an ^{18}F-FDG PET/CT scan?	
6	If the patient is an adult DM patient with anti-TIF1-gamma positivity with disease onset >40 years and ≥1 additional high risk clinical feature, have they undergone an ^{18}F-FDG PET/CT scan as a single screening investigation?	
7	If the patient is an adult at high risk of IIM-related cancer and cancer has not been detected via investigations at the time of IIM diagnosis, have they undergone upper and lower gastro-intestinal endoscopy?	
8	If the patient is from a geographical region where risk of nasopharyngeal carcinoma is increased, have they undergone naso-endoscopy at the time of IIM diagnosis?	

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