

# **Development and evaluation of a register-based organ damage index in systemic lupus erythematosus: a nationwide, population-based study from Sweden**

Alvaro Gomez<sup>1</sup>, Ioannis Parodis<sup>1,2</sup>, Muna Saleh<sup>3</sup>, Julia F. Simard<sup>4,5</sup>, Christopher Sjöwall<sup>3</sup>, Elizabeth V. Arkema<sup>5</sup>

<sup>1</sup>Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden.

<sup>2</sup>Department of Rheumatology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden.

<sup>3</sup>Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Sweden.

<sup>4</sup>Department of Epidemiology and Population Health; Division of Immunology and Rheumatology, Department of Medicine, Stanford University School of Medicine, Stanford, California, USA.

<sup>5</sup>Clinical Epidemiology Division, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden.

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**Supplemental Table S1.** Item definition for the register-based organ damage index (RBODI)

SDI Item	Clinical diagnoses (ICD-10 codes)	Medical procedures (KVÅ codes)	Surgical procedures (KVÅ and DRG codes)	Prescriptions (ATC codes)
OCULAR				
Any cataract ever	H25, Senile cataract H26, Other cataract H28, Cataract and other disorders of lens in diseases classified elsewhere		CJC, Intracapsular cataract extraction CJD, Extracapsular cataract extraction CJE, Extracapsular cataract extraction with phacoemulsification	
Retinal change OR optic atrophy	H32, Chorioretinal disorders in diseases classified elsewhere H34, Retinal vascular occlusions H35.0 Background retinopathy and retinal vascular changes H35.2, Other proliferative retinopathy H35.3, Degeneration of macula and posterior pole) H35.4, Peripheral retinal degeneration H35.6, Retinal haemorrhage			

	H35.7, Separation of retinal layers H35.8, Other specified retinal disorders H35.9, Retinal disorder, unspecified H36, Retinal disorders in diseases classified elsewhere H47.2, Optic atrophy H48.0, Optic atrophy in diseases classified elsewhere H48.1, Retrobulbar neuritis in diseases classified elsewhere			
NEUROPSYCHIATRIC				
Cognitive impairment (e.g., memory deficit, difficulty with calculation, poor concentration, difficulty in spoken or written language, impaired performance level)  OR major psychosis	<b>Cognitive impairment:</b>  F00, Dementia in Alzheimer disease F01, Vascular dementia F02, Dementia in other diseases classified elsewhere F03, Unspecified dementia F04, Organic amnesic syndrome, not induced by alcohol and other psychoactive substances F05.1, Delirium superimposed on dementia G30, Alzheimer disease			

	<p>G31.1, Senile degeneration of brain, not elsewhere classified</p> <p>G31.8A, Degenerative disorders in Lewy body dementia</p> <p>Excluding: F70-F79, Mental retardation</p>			
	<p><b>Major psychosis:</b></p> <p>F20, Schizophrenia</p> <p>F22, Persistent delusional disorders</p> <p>F25, Schizoaffective disorders</p> <p>Excluding: F70-F79, Mental retardation</p>			<p><b>Major psychosis:</b></p> <p>N05AH02, Clozapine</p> <p>[Two or more prescriptions, at least six months apart]</p>
Seizures requiring therapy for 6 months (1)	<p>G40, Epilepsy</p> <p>G41, Status epilepticus</p>			<p>N03, Antiepileptics</p> <p>[Two or more prescriptions, at least six months apart]</p> <p>[Definition requires clinical diagnosis and prescription]</p>
Cerebral vascular accident ever	I60, Subarachnoid haemorrhage			

(score 2 if > 1), or resection not for malignancy (2)	I61, Intracerebral haemorrhage I63, Cerebral infarction I64, Stroke, not specified as haemorrhage or infarction G45, Transient cerebral ischaemic attacks and related syndromes			
Cranial or peripheral neuropathy (excluding optic)	E11.4, Type 2 diabetes mellitus – with neurological complications G50, Disorders of trigeminal nerve G51, Facial nerve disorders G52, Disorders of other cranial nerves G53, Cranial nerve disorders in diseases classified elsewhere  G57.2, Lesion of femoral nerve G57.3, Lesion of lateral popliteal nerve G57.4, Lesion of medial popliteal nerve G58.7, Mononeuritis multiplex G58.8, Other specified mononeuropathies G58.9, Mononeuropathy, unspecified  G59, Mononeuropathy in diseases classified elsewhere			

	G61, Inflammatory polyneuropathy G62, Other polyneuropathies G63, Polyneuropathy in diseases classified elsewhere G64, Other disorders of peripheral nervous system			
Transverse myelitis	G37.3, Acute transverse myelitis in demyelinating disease of central nervous system			
RENAL				
Estimated or measured GFR <50 %	N18.4, Chronic kidney disease, stage 4			
Proteinuria 24 h >3.5 g OR End-stage renal disease (regardless of dialysis or transplantation)	<b>ESRD:</b> N18.5, Chronic kidney disease, stage 5  <b>Renal transplant:</b> Z94.0, Kidney transplant status  <b>Renal dialysis:</b> Z99.2, Dependence on renal dialysis	<b>Renal dialysis:</b> DR016, Haemodialysis, chronic  DR024, Peritoneal dialysis, chronic  DR061, Start of haemodialysis	<b>Renal transplant:</b> KAS00, Autologous kidney transplantation  KAS10, Open transplantation of kidney from deceased donor  KAS20, Open transplantation of kidney from living donor	
PULMONARY				

Pulmonary hypertension (right ventricular prominence, or loud P2) (4)	I27.0, Primary pulmonary hypertension  I27.2, Other secondary pulmonary hypertension  I27.9, Pulmonary heart disease, unspecified			
Pulmonary fibrosis (physical and X-ray)	J70.1, Chronic and other pulmonary manifestations due to radiation  J70.3, Chronic drug-induced interstitial lung disorders  J84.1, Other interstitial pulmonary diseases with fibrosis			
Shrinking lung (X-ray)				
Pleural fibrosis (X-ray)	J92, Pleural plaque  J94.1, Fibrothorax			
Pulmonary infarction (X-ray) OR resection not for malignancy	I26, Pulmonary embolism		GDB, Lung resection excluding C34, Malignant neoplasm of bronchus and lung	
CARDIOVASCULAR				
Angina OR coronary artery bypass	<b>Angina</b>  I20, Angina pectoris  I24, Other acute ischaemic heart diseases I25, Chronic ischaemic heart disease			



	<b>CABG</b> Z95.1, Presence of aortocoronary bypass graft Z95.5, Presence of coronary angioplasty implant and graft		<b>CABG</b> FNA, Anastomosis between internal thoracic artery and coronary arteries FNB, Anastomosis between gastroepiploic artery and coronary arteries FNC, Aortocoronary vein bypass FND, Aortocoronary bypass with vascular prosthesis FNE, Coronary bypass with free artery grafts FNG, Dilatation and recanalisation of coronary artery	
Myocardial infarction ever (score 2 if > 1) (5)	I21, Acute myocardial infarction I22, Subsequent myocardial infarction			
Cardiomyopathy (ventricular dysfunction)	I25.5, Ischaemic cardiomyopathy I42, Cardiomyopathy			
Valvular disease (diastolic murmur,	I05, Rheumatic mitral valve diseases I06, Rheumatic aortic valve diseases		FG, Tricuspid valve surgery	

or a systolic murmur > 3/6)	I07, Rheumatic tricuspid valve diseases I08, Multiple valve diseases I34, Nonrheumatic mitral valve disorders I35, Nonrheumatic aortic valve disorders I36, Nonrheumatic tricuspid valve disorders I37, Pulmonary valve disorders  Z95.2, Presence of prosthetic heart valve Z95.3, Presence of xenogeneic heart valve Z95.4, Presence of other heart-valve replacement		FK, Mitral valve surgery  FM, Aortic valve surgery  FJE, Surgery for isolated pulmonary stenosis  FJF, Implantation of pulmonary valve prosthesis	
Pericarditis x 6 months or pericardiectomy	I09.2, Chronic rheumatic pericarditis I31.0, Chronic adhesive pericarditis I31.1, Chronic constrictive pericarditis		FEB, Pericardiotomy  FEF, Resection and extirpation of the pericardium	
PERIPHERAL VASCULAR				
Claudication x 6 months	I73.9B, Intermittent claudication			B01AC23, cilostazol  CO4AD03, pentoxifylline  [Two or more prescriptions, at least six months apart]

Minor tissue loss (pulp space)	I73.9C Digital ischaemia			
Significant tissue loss ever (e.g., loss of digit or limb, resection) (score 2 if > 1)			<p>[KVÅ]</p> <p>NHQ, Amputation and related operations on ankles and feet</p> <p>[DRG]</p> <p>E20, 113, 114, Amputations due to circulatory diseases, other than upper limb or toe</p> <p>E21, Upper limb or toe amputations due to circulatory diseases</p> <p>H09, Amputation for muscle, bone or connective tissue disorders</p> <p>L01, Lower limb amputation for endocrine, nutritional &amp; metabolic diseases</p>	
Venous thrombosis with swelling,	I80, Phlebitis and thrombophlebitis I81, Portal vein thrombosis			

ulceration, OR venous stasis (6)	I82, Other venous embolism and thrombosis			
GASTROINTESTINAL				
Infarction or resection of bowel (below duodenum), spleen, liver or gall bladder ever (score 2 if >1)	<b>Bowel:</b>  K55.0, Acute vascular disorders of intestine  <b>Spleen:</b>  D73.5, Infarction of spleen  <b>Liver:</b>  K76.3, Infarction of liver		<b>Bowel:</b>  [KVÅ]  JFB, Resection of small bowel and colon  JFH, Colectomy  [DRG]  FO1, 146, 147, Rectal resection and extirpation  FO5, 148, 149, Major small and large bowel surgery  FO9, 152, 153, Minor small and large bowel surgery  F30, 166, 167, Appendectomy  <b>Spleen:</b>  [KVÅ]  JMA, Spleen resection and splenectomy	

			<p>[DRG]</p> <p>R01N, 392, 393O, Spleen extirpation</p> <p><b>Liver:</b></p> <p>[KVÅ]</p> <p>JJB, Liver resection</p> <p>[DRG]</p> <p>G01N, 480, Liver transplant</p> <p><b>Gallbladder:</b></p> <p>[KVÅ]</p> <p>JKA20, Cholecystectomy</p> <p>JKA21, Laparoscopic cholecystectomy</p> <p>[DRG]</p> <p>G10, 196, 196, Cholecystectomy with choledochal exploration</p> <p>G11, 197, 198, Open cholecystectomy</p>	
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			without choledochal exploration  G12, 493, 494, Laparo/endoscopic biliary surgery  G30, 4940, Cholecystectomy and biliary tract surgery	
Mesenteric insufficiency	K55.1, Chronic vascular disorders of intestine			
Chronic peritonitis	K65.8, Other peritonitis  N73.4, Female chronic pelvic peritonitis			
Stricture OR upper gastrointestinal tract surgery ever	K22.2, Oesophageal obstruction		[KVÅ]  JC, Oesophageal surgery  JD, Stomach and duodenum surgery  [DRG]  LO8, 288, Gastrointestinal surgery for obesity  F11, 154–156, Major surgery of the stomach, oesophagus and duodenum  F12, Other operations of the stomach,	

			oesophagus and duodenum  F130, Surgery of the stomach, oesophagus and duodenum  F35, 170, 171 Other operations for gastrointestinal diseases	
Pancreatic insufficiency requiring enzyme replacement or with pseudocyst	K86.0, Alcohol-induced chronic pancreatitis  K86.1, Other chronic pancreatitis  K86.3, Pseudocyst of pancreas  K86.8, Other specified diseases of pancreas  K86.9, Disease of pancreas, unspecified  E16.9, Disorder of pancreatic internal secretion, unspecified			A09AA02, multienzymes (lipase, protease, etc)  [Definition requires clinical diagnosis or prescription + K86.8, K86.9, K90.3, E16.9]
MUSCULOSKELETAL				
Atrophy or weakness	M62.5, Muscle wasting and atrophy, not elsewhere classified			
Deforming or erosive arthritis (including reducible deformities, excluding	M12.0, Chronic postrheumatic arthropathy [Jaccoud]			

avascular necrosis)	<p>M05.8L Erosive rheumatoid arthritis, RF-positive and ACPA-positive,</p> <p>M05.8M Erosive rheumatoid arthritis, RF-positive and ACPA-negative</p> <p>M05.8N Erosive rheumatoid arthritis, RF-positive and ACPA-unspecified</p> <p>M06.8L Erosive rheumatoid arthritis, RF-negative and ACPA-positive,</p> <p>M06.8M Erosive rheumatoid arthritis, RF-negative and ACPA-positive,</p> <p>M06.8N Erosive rheumatoid arthritis, RF-negative and ACPA-positive</p>			
Osteoporosis with fracture or vertebral collapse (excluding avascular necrosis) (7)	<p><b>Osteoporosis:</b></p> <p>M80, Osteoporosis with pathological fracture</p> <p>M81, Osteoporosis without pathological fracture</p> <p>M82, Osteoporosis in diseases classified elsewhere</p> <p><b>Non-vertebral fracture:</b></p> <p>S12, Fracture of neck</p> <p>S22, Fracture of rib(s), sternum and thoracic spine</p>			<p>G03XC01, Tibolone</p> <p>HO5AA02, Teriparatide</p> <p>M05BA, Bisphosphonates</p> <p>M05BB, Bisphosphonates combinations</p> <p>M05BX03, Strontium ranelate</p> <p>M05BX04, Denosumab</p> <p>[Two or more prescriptions, at least six months apart]</p>



	<p>S32, Fracture of lumbar spine and pelvis</p> <p>S42, Fracture of shoulder and upper arm</p> <p>S52, Fracture of forearm</p> <p>S62, Fracture at wrist and hand level</p> <p>S72, Fracture of femur</p> <p>S82, Fracture of lower leg, including ankle</p> <p>S92, Fracture of foot, except ankle</p> <p>T02, Fractures involving multiple body regions</p> <p>T08, Fracture of spine, level unspecified</p> <p>T10, Fracture of upper limb, level unspecified</p> <p>T12, Fracture of lower limb, level unspecified</p> <p>T14.2, Fracture of unspecified body region</p> <p><b>Vertebral collapse:</b></p> <p>M48.5, Collapsed vertebra, not elsewhere classified</p> <p>S12.0, Fracture of first cervical vertebra</p> <p>S12.1, Fracture of second cervical vertebra</p> <p>S12.2, Fracture of other specified cervical vertebra</p>			
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	S22.0, Fracture of thoracic vertebra S22.1, Multiple fractures of thoracic spine S32.0, Fracture of lumbar vertebra  [Definition requires a code for osteoporosis and at least one code for non-vertebral fracture or vertebral collapse].			
Avascular necrosis (score 2 if > 1)	M87.0, Idiopathic aseptic necrosis of bone M87.3, Other secondary osteonecrosis M87.8, Other osteonecrosis M87.9, Osteonecrosis, unspecified			
Osteomyelitis	M86, Osteomyelitis			
Ruptured tendons	M66.2, Spontaneous rupture of extensor tendons M66.3, Spontaneous rupture of flexor tendons M66.4, Spontaneous rupture of other tendons M66.5, Spontaneous rupture of unspecified tendon			
SKIN				

Alopecia	L66, Cicatricial alopecia [scarring hair loss]			
Extensive scarring or paniculum other than scalp and pulp space	L90.5, Scar conditions and fibrosis of skin			
Skin ulceration (excluding thrombosis) for more than 6 months	<p>E10.6D, Type 1 diabetes mellitus with foot ulcer</p> <p>E11.6D, Type 2 diabetes mellitus with foot ulcer</p> <p>I70.2C, Atherosclerosis of native arteries of the extremities with ulcer</p> <p>I83.0, Varicose veins of lower extremities with ulcer</p> <p>I83.2, Varicose veins of lower extremities with both ulcer and inflammation</p> <p>L89, Pressure ulcer</p> <p>L97, Ulcer of lower limb, not elsewhere classified</p> <p>[Two or more codes, at least six months apart]</p> <p>L98.4, Chronic ulcer of skin, not elsewhere classified</p>			

<p>PREMATURE GONADAL FAILURE (8)</p>	<p>E28.3, Primary ovarian failure E89.4, Postprocedural ovarian failure</p>			<p>Prescription to women younger than 40</p> <p>G03CA03, oestradiol</p> <p>G03CA57, conjugated oestrogens</p> <p>G03CX01, tibolone</p> <p>G03FA01, norethisterone and oestrogen</p> <p>G03FA12 medroxyprogesterone and oestrogen</p> <p>G03FA15, dienogest and oestrogen</p> <p>G03FA17, drospirenone and oestrogen</p> <p>G03FB05, norethisterone and oestrogen</p> <p>G03FB06 medroxyprogestgerone and oestrogen</p> <p>G03FB09 levonorgestrel and oestrogen</p>
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				[Two or more prescriptions, at least six months apart]
DIABETES	E10, Type 1 diabetes mellitus E11, Type 2 diabetes mellitus E12, Malnutrition-related diabetes mellitus E13, Other specified diabetes mellitus E14, Unspecified diabetes mellitus			A10, Drugs used in diabetes (9)  [Two or more prescriptions, at least six months apart]
MALIGNANCY (exclude dysplasia) (9)	C00-C97, Malignant neoplasms (excluding C44, Other malignant neoplasms of skin)  D00-D09, In situ neoplasms			

**Supplemental Table S2.** Accuracy measurements of RBODI to detect the presence of organ damage related to or independent of glucocorticoid use according to SDI in SLE cases from Östergötland, Sweden 2021 (N=271).

Item	RBODI, n (%)	SDI, n (%)	Se (95% CI)	Sp (95% CI)	PPV (95% CI)	NPV (95% CI)
GC-related	129 (47.6)	142 (52.4)	0.80 (0.73, 0.86)	0.88 (0.82, 0.93)	0.88 (0.82, 0.93)	0.80 (0.73, 0.86)
GC-definite	80 (29.5)	83 (30.6)	0.76 (0.65, 0.85)	0.91 (0.86, 0.95)	0.79 (0.68, 0.87)	0.90 (0.84, 0.93)
GC-possible	85 (31.4)	109 (40.2)	0.69 (0.59, 0.77)	0.94 (0.89, 0.97)	0.88 (0.79, 0.94)	0.82 (0.75, 0.94)
GC-independent	69 (25.5)	98 (36.2)	0.61 (0.51, 0.71)	0.95 (0.90, 0.98)	0.87 (0.77, 0.94)	0.81 (0.75, 0.86)

GC-definite domains: ocular, musculoskeletal.

GC-possible domains: cardiovascular, peripheral vascular, neuropsychiatric, diabetes.

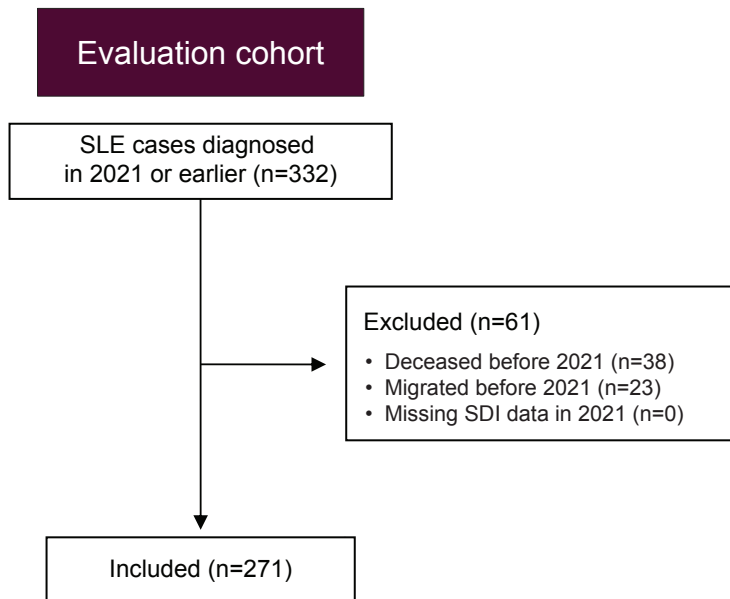
GC-independent domains: renal, pulmonary, gastrointestinal, skin, gonadal, malignancy.

GC, glucocorticoid; NPV, negative predictive value; PPV, positive predictive value; RBODI, register-based organ damage index; SDI, SLICC/ACR damage index; Se, sensitivity; SLE, systemic lupus erythematosus; Sp, specificity.

**Supplemental Table S3.** Cumulative incidence at 5 years after diagnosis for all RBODI organ domains by sex.

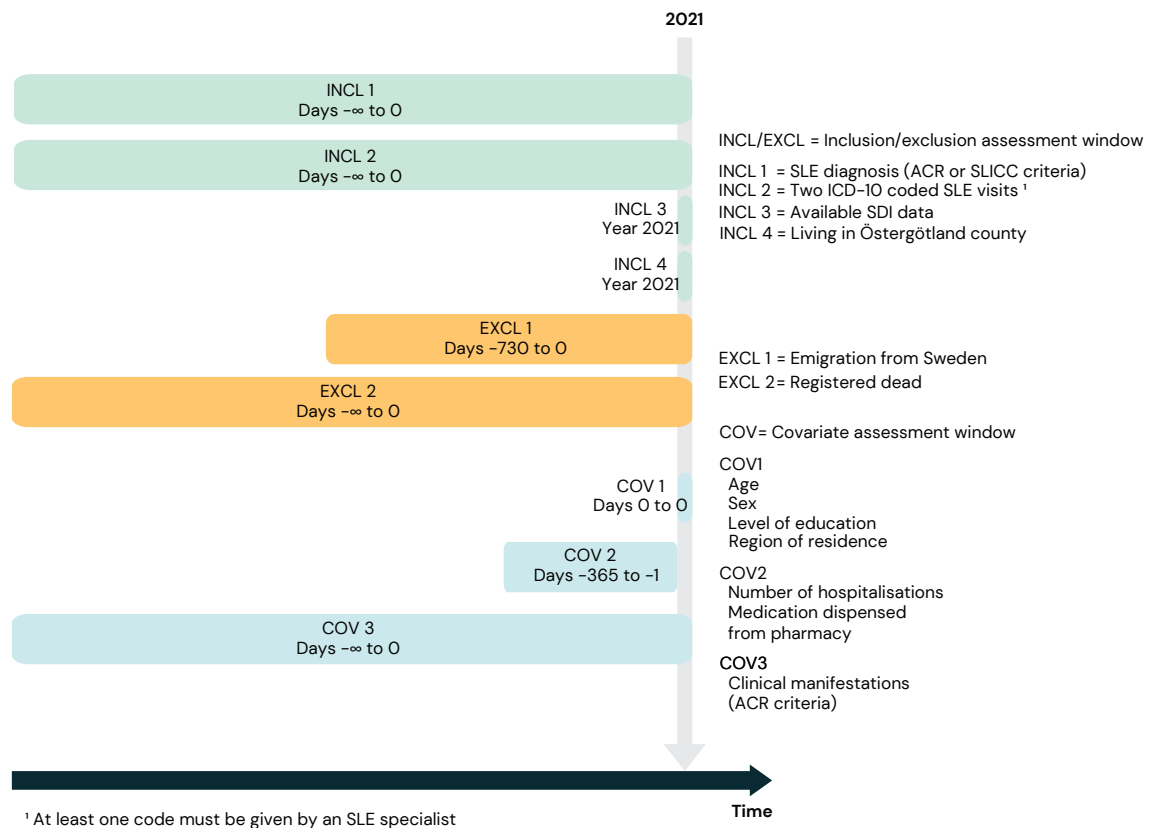
	<b>Overall (N=4441)</b>	<b>Female (N=3661)</b>	<b>Male (N=780)</b>
Ocular	0.140 (0.129–0.152)	0.128 (0.116–0.139)	0.202 (0.170–0.233)
Neuropsychiatric	0.087 (0.078–0.096)	0.074 (0.065–0.083)	0.116 (0.091–0.141)
Renal	0.025 (0.021–0.030)	0.020 (0.016–0.025)	0.050 (0.033–0.066)
Pulmonary	0.047 (0.040–0.053)	0.045 (0.037–0.052)	0.056 (0.038–0.073)
Cardiovascular	0.079 (0.070–0.087)	0.064 (0.056–0.073)	0.148 (0.121–0.175)
Peripheral vascular	0.046 (0.039–0.052)	0.039 (0.033–0.046)	0.075 (0.055–0.095)
Gastrointestinal	0.047 (0.040–0.054)	0.045 (0.038–0.053)	0.054 (0.036–0.072)
Musculoskeletal	0.043 (0.036–0.049)	0.043 (0.036–0.050)	0.041 (0.025–0.057)
Mucocutaneous	0.006 (0.004–0.009)	0.008 (0.005–0.011)	0.010 (0.003–0.018)
Premature gonadal failure	0.002 (0.001–0.003)	0.002 (0.001–0.004)	N/A
Diabetes	0.047 (0.041–0.054)	0.042 (0.035–0.049)	0.073 (0.054–0.093)
Malignancy	0.068 (0.060–0.076)	0.063 (0.055–0.072)	0.090 (0.067–0.112)

**Supplemental Figure S1.** Flow diagram of participant disposition in the evaluation cohort

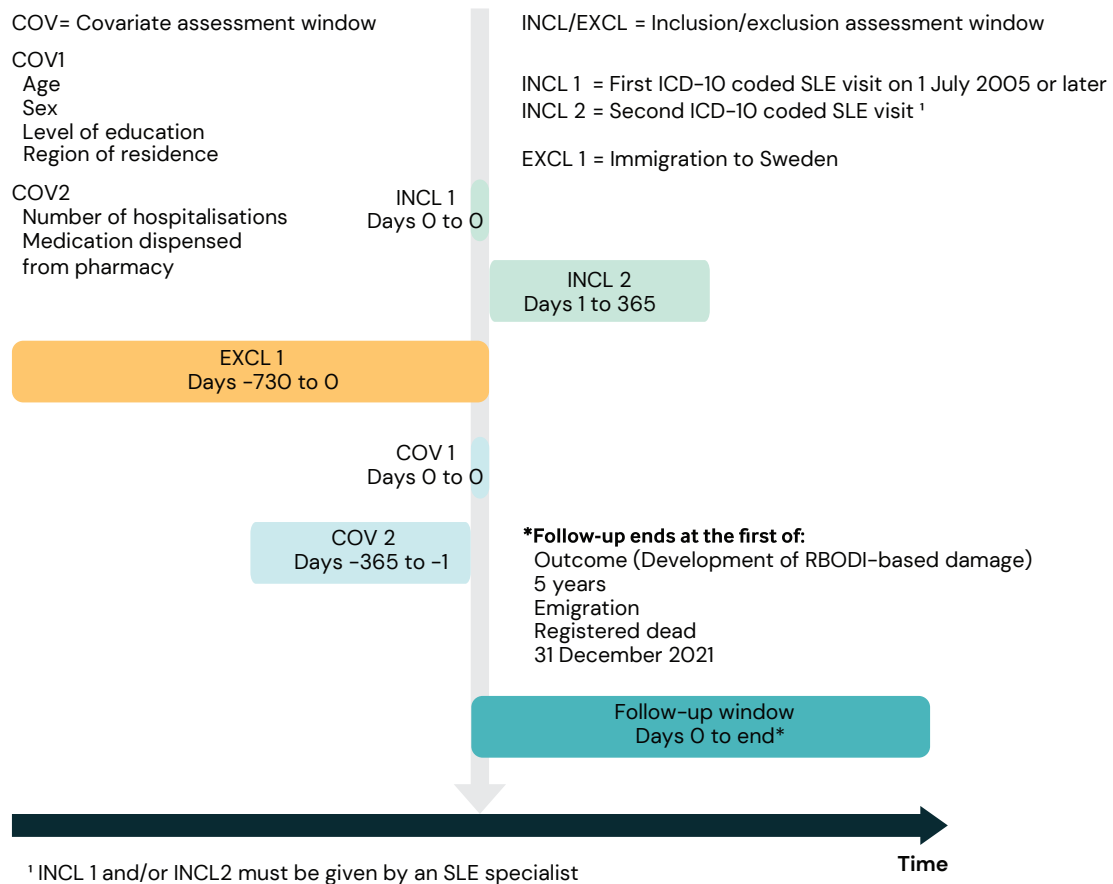




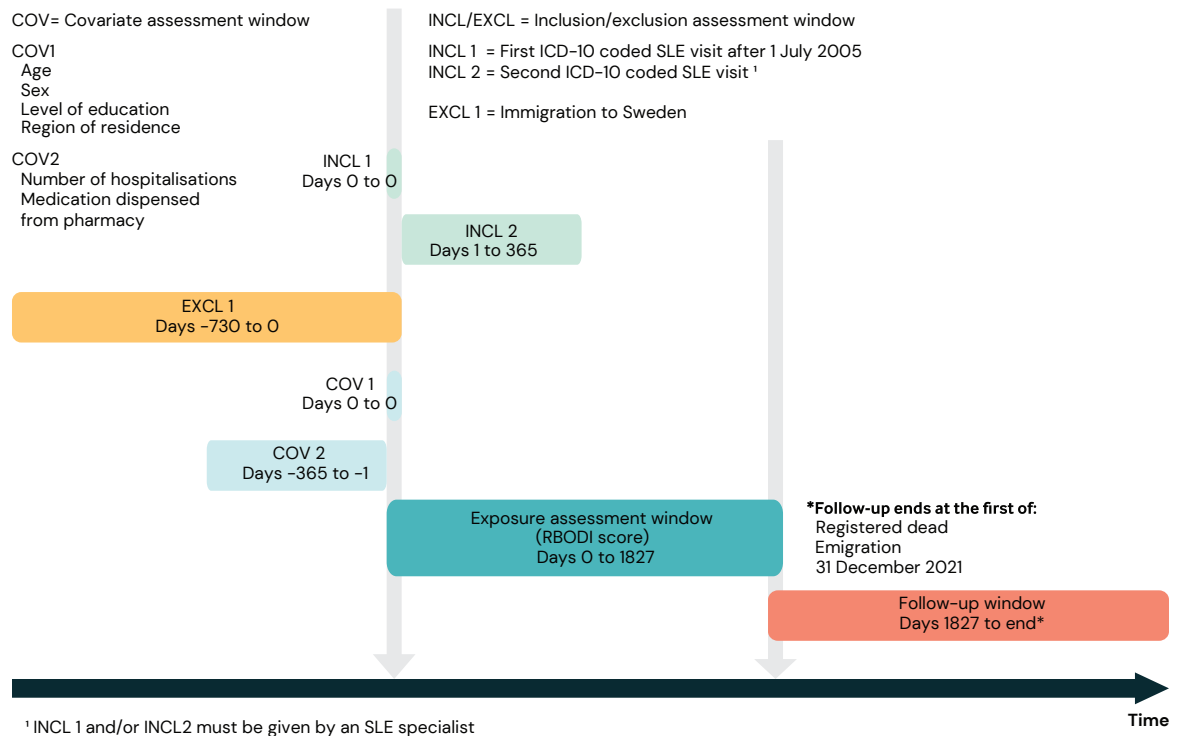
**Supplemental Figure S2. Study design diagram for the validation of RBODI.**



**Supplemental Figure S3.** Study design diagram for organ damage occurrence in the nationwide cohort of newly diagnosed SLE patients.



**Supplemental Figure S4.** Study design diagram for the association between organ damage accrual and mortality risk in the nationwide cohort of newly diagnosed SLE patients.



**Supplemental Figure S5.** Cumulative incidence at five years after diagnosis for all organ damage domains in newly diagnosed patients with SLE in Sweden (N=4441).

