

Supplementary Table I. Baseline characteristics of included studies (n = 24)

Author, year, ref.	Country/region	Study design	Study period	Sample size (SS)	Sample size (controls)	Total patients	SS definition	Mean Age [years]	Female [%]	Disease duration	Comparator group	Matching criteria	Primary outcomes	Secondary outcomes	Follow-up period	Loss to follow-up	Effect size (95% CI)	Heterogeneity (I ²)	Quality Score (NOS)	Key Findings	Subgroup analysis	Limitations
Ungprasert et al. 2015 [1]	International	Systematic review and meta-analysis	Up to 2014	5 studies pooled	General population	~15,000	Various criteria (AECG 2002, others)	50-60 (pooled)	90-95%	Variable	General population	Age, sex, standardization	VTE (DVT, PE combined)	DVT alone, PE alone	Variable (3-10 years)	Variable	RR 2.05 (1.86-2.27)	42% (moderate)	High quality meta-analysis	Doubled VTE risk; moderate heterogeneity	By geography, study design	Heterogeneous populations, limited adjustment
Aviña-Zubieta et al. 2017 [2]	Canada (British Columbia)	Population-based cohort	1996-2010	1,175	11,750	12,925	ICD-9 codes + physician diagnosis	57.2 ±14.8	89.4%	New diagnosis	General population	Age, sex, entry time (10:1)	VTE (combined DVT/PE)	DVT, PE separately	Mean 8.1 years (max 15)	2.1%	VTE aHR 2.92 (1.66-5.16)	N/A	8/9 (low risk)	Highest risk in first year post-diagnosis	By time since diagnosis, age groups	Administrative data, potential misclassification
Sun et al. 2023 [3]	Denmark	Nationwide registry cohort	1996-2018	5,092	20,368	25,460	ICD-10 codes (M35.0)	58.3 ±16.2	88.7%	Incident cases	General population	Age, sex, comorbidities (4:1)	Heart failure	VTE, MACE, mortality	Median 7.4 years (IQR 3.2-12.8)	<1%	HF aHR 1.42 (1.20-1.68)	N/A	8/9 (low risk)	10-year HF incidence: 4.0% vs 2.8%	By age, sex, comorbidities	Registry data, no serological markers
Loiseau et al. 2025 [4]	Denmark	Nationwide cohort	1996-2017	4,697	46,970	51,667	ICD-10 codes + hospital registries	59.1 ±17.4	87.3%	Incident and prevalent	General population	Age, sex, calendar year (10:1)	VTE (DVT, PE)	MI, ischemic/hemorrhagic stroke, PAD	Median 7.6 years (max 23)	Minimal	VTE aHR 1.57 (1.33-1.85)	N/A	9/9 (low risk)	Largest cohort; comprehensive outcomes	By age, sex, calendar period	Registry data, no disease activity measures
Chiang et al. 2014 [5]	Taiwan	Nationwide cohort	2000-2010	4,276	42,760	47,036	ICD-9 codes (710.2)	53.8 ±14.9	92.1%	Incident cases	General population	Age, sex, comorbidities (10:1)	Ischemic stroke	Stroke subtypes	Mean 3.7 years	1.8%	Stroke aHR 1.34 (1.15-1.56)	N/A	7/9 (moderate risk)	Increased stroke risk in younger patients	By age groups, stroke subtypes	Administrative codes, no serological data
Wu et al. 2018 [6]	Taiwan	Nationwide cohort	2002-2013	4,175	16,700	20,875	ICD-9 codes (710.2)	52.4 ±15.2	90.8%	Incident cases	General population	Age, sex, index date (4:1)	Coronary heart disease	Acute MI, angina pectoris	Mean 6.7 years	2.3%	CHD aHR 1.52 (1.23-1.87)	N/A	7/9 (moderate risk)	52% increased CHD risk	By age, sex, comorbidities	Claims data, no disease severity
Bartoloni et al. 2015 [7]	Italy	Multicentre cohort	2009-2013	367	367	734	2002 AECG criteria	54.6 ±12.8	94.2%	8.4 ± 6.7 years	Hospital-based controls	Age, sex (1:1)	Any cardiovascular disease	MI, stroke, PAD	Mean 5.2 years	3.8%	CVD OR 3.9 (2.1-7.1)	N/A	8/9 (low risk)	Extraglandular disease increases risk	By disease activity, serology	Hospital controls, selection bias
Yong et al. 2018 [8]	International	Systematic review & meta-analysis	Up to 2017	8 studies pooled	General population	~35,000	Various criteria (AECG, ACR/EULAR)	50-65 (pooled)	85-95%	Variable	General population	Study-specific matching	Ischemic stroke	Cardiovascular disease	Variable (2-15 years)	Variable	Stroke aHR 0.84 (0.63-1.12)	Low heterogeneity	High quality meta-analysis	No significant stroke risk overall	By study design, geography	Heterogeneous populations, adjustment varies
Beltai et al. 2020 [9]	International	Systematic review & meta-analysis	Up to 2018	67,124 SS patients	General population	> 500,000	Various criteria	45-65 (pooled)	85-95%	Variable	General population	Study-specific	CV morbidity and mortality	VTE, stroke, MI	Variable (1-20 years)	Variable	RR 1.78 for thromboembolic events	Moderate to high	High quality meta-analysis	Broad CV and VTE risk synthesis	By outcome type, study quality	High heterogeneity, varied definitions
Zippel et al. 2022 [10]	Germany	Hospital registry cohort	2010-2020	312	312	624	Clinical diagnosis + serology	48.3 ±8.7	91.7%	6.2 ± 4.9 years	Hospital-based controls	Age, sex (1:1)	Premature stroke (<55 years)	CV risk factors	Mean 3.8 years	5.1%	Stroke OR 2.1 (1.3-3.2)	N/A	7/9 (moderate risk)	Elevated stroke risk <55 years	By age groups, serology	Single center, hospital controls
Pérez-De-Lis et al. 2010 [11]	Spain	Case-control study	2005-2008	624	624	1,248	2002 AECG criteria	56.4 ±14.2	93.8%	9.1 ± 7.3 years	Healthy volunteers	Age, sex (1:1)	CV risk factors	Hypertension, hyperlipidemia	Cross-sectional	N/A	HTN OR 1.4; Hyperlipidemia OR 1.3	N/A	6/9 (moderate risk)	Traditional CV risk factor analysis	By disease activity, serology	Cross-sectional, selection bias
Rochette et al. 2025 [12]	France	Nationwide retrospective cohort	2012-2020	1,324	6,620	7,944	ICD-10 codes + VTE history	62.8 ±15.4	86.9%	Variable	VTE patients without autoimmune disease	Age, sex, VTE type (5:1)	Recurrent VTE	VTE-related mortality	Mean 5.1 years	2.7%	1-year recurrence aHR 1.85 (1.45-2.36)	N/A	8/9 (low risk)	Novel VTE recurrence risk study	By VTE type, anticoagulation	Administrative data, no disease activity
Su et al. 2024 [13]	International (GWAS)	Two-sample Mendelian randomization	GWAS data up to 2023	SS GWAS: 2,818 cases	CV GWAS: 463,010 controls	465,828	Genetic variants (SNPs)	Not applicable	Mixed population	N/A (genetic study)	GWAS population controls	Genetic ancestry matching	Causal CV associations	Stroke, heart failure	N/A (genetic analysis)	N/A	Stroke OR 1.18; HF OR 1.24	Low pleiotropy	High quality MR	Genetic causal evidence for CV risk	By genetic instrument strength	Population stratification, pleiotropy
Lin et al. 2022 [14]	Taiwan	Health claims cohort	2000-2013	2,847	11,388	14,235	ICD-9 codes (710.2)	54.3 ±13.7	91.2%	Incident cases	General population	Age, sex, index date (4:1)	Incident heart failure	HF subtypes	Mean 7.4 years	1.9%	HF aHR 1.45 (1.22-1.72)	N/A	7/9 (moderate risk)	45% increased HF risk	By age, comorbidities	Administrative data, no echocardiography
Caraba et al. 2023 [15]	Romania	Cross-sectional biomarker study	2021-2022	89	45	134	2016 ACR/EULAR criteria	58.7 ±12.4	94.4%	7.8 ± 5.2 years	Healthy volunteers	Age, sex matching	Endothelial dysfunction biomarkers	FMD, D-dimer, vWF	Cross-sectional	N/A	FMD +3.8%; D-dimer +42%	N/A	6/9 (moderate risk)	Biomarkers correlate with disease activity	By disease activity scores	Small sample, cross-sectional design
Chandra et al. 2022 [16]	India	Case report	2022	1	N/A	1	Clinical diagnosis + serology	35	100% (1 female)	New diagnosis	N/A	N/A	Cerebral venous thrombosis	Treatment response	3 months	N/A	Case description	N/A	Case report quality	CVT as initial SS presentation	N/A	Single case, limited follow-up

Liu et al. 2023 [17]	China	Case series + literature review	2018–2022	6	Literature comparison	6	Clinical diagnosis + ANA/RF	42.3 ±14.8	83.3%	Variable (2-8 years)	Literature cases	Literature comparison	CVT clinical features	Treatment outcomes	Mean 6 months	16.7 % (1/6)	Recovery rate 83.3%	N/A	Case series quality	5/6 patients full recovery with treatment	By treatment modality	Small sample, retrospective
Ho et al. 2016 [18]	Taiwan	Case report	2016	1	N/A	1	Clinical + atypical antibodies	48	100% (1 female)	10 years	N/A	N/A	CVT with atypical serology	Neurological recovery	6 months	N/A	Case description	N/A	Case report quality	CVT with atypical antibodies	N/A	Single case, atypical presentation
Zhou et al. 2023 [19]	International	Literature review	2000–2022	Review of multiple studies	Literature comparison	Multiple cohorts	Various criteria	Variable	Variable	Variable	Other autoimmune diseases	Literature-based	CVT patterns in autoimmune diseases	Treatment outcomes	Variable	Variable	Descriptive review	N/A	Narrative review quality	CVT patterns across autoimmune conditions	By disease type	Narrative review, heterogeneous data
Rajasekhar et al. 2024 [20]	India	Case report	2023	1	N/A	1	Clinical diagnosis	32	100% (1 female)	5 years	N/A	N/A	Ischemic stroke in young woman	Stroke recovery	3 months	N/A	Case description	N/A	Case report quality	Young woman (<40 yrs) with pSS stroke	N/A	Single case, young age atypical
Carvalho et al. 2021 [21]	International	Case-based review	Literature review	Multiple cases	Literature comparison	Multiple case reports	Various criteria	Variable	Variable	Variable	General TTP literature	Literature-based	TTP in SS patients	ADAMTS-13 levels	Variable	Variable	Descriptive review	N/A	Review quality	ADAMTS-13 deficiency mechanisms	By treatment response	Case-based review, rare condition
Atzeni et al. 2022 [22]	International	Narrative review	Literature up to 2021	Literature review	N/A	Multiple studies	Various criteria	N/A	N/A	N/A	N/A	N/A	CV involvement mechanisms	Pathophysiological pathways	N/A	N/A	Mechanistic review	N/A	Narrative review quality	Interferon-mediated vasculopathy pathways	By mechanism type	Narrative review, limited systematic approach
Sisto et al. 2022 [23]	International	Mechanistic review	Literature up to 2022	Literature review	N/A	Multiple studies	Various criteria	N/A	N/A	N/A	N/A	N/A	Molecular pathways	Therapeutic targets	N/A	N/A	Pathway analysis	N/A	Review quality	Inflammation→autoimmunity→thrombosis pathways	By pathway type	Review format, limited clinical correlation
Brito-Zerón et al. 2017 [24]	International	Book chapter	Literature up to 2016	Literature review	N/A	Multiple studies	Various criteria	N/A	N/A	N/A	N/A	N/A	CV involvement overview	Clinical manifestations	N/A	N/A	Descriptive overview	N/A	Book chapter quality	Comprehensive CV involvement patterns	By manifestation type	Book chapter, not peer-reviewed research

AECG – American-European Consensus Group, ACR – American College of Rheumatology, aHR – adjusted hazard ratio, CHD – coronary heart disease; CVD – cardiovascular disease, CVT – cerebral venous thrombosis, FMD – flow-mediated dilation, CV – cardiovascular, EULAR – European Alliance of Associations for Rheumatology, HF – heart failure, ICD – International Classification of Diseases, MI – myocardial infarction, OR – odds ratio, RR – relative risk, SjD – Sjögren's disease, TTP – thrombotic thrombocytopenic purpura, VTE – venous thromboembolism.

