

## SUPPLEMENTARY MATERIALS

**Table S1.** List of diagnosis for disease identification and patients' characterisation

	ICD9-CM
<b>Main inclusion criteria</b>	
Systemic lupus erythematosus	710.0
Cutaneous only lupus	695.4, 373.34
<b>EULAR/ACR criteria</b>	
Leukopenia	288.50, 288.59
Thrombocytopenia	287.3, 287.4, 287.5
Autoimmune haemolysis	283.0
Delirium	297
Psychosis	290-299
Seizure	333.2, 345.0-345.9
Non-scarring alopecia	704.0
Oral ulcers	528.0
Acute pericarditis	420
Pleural and pericardial effusion	510.9, 511, 391.0, 393,423.1, 423.2
<b>Exclusion criteria</b>	
Primary vasculitis	446, 447.5
Myositis	729.1
Polymyositis	710.4
Dermatomyositis	710.3
Psoriatic arthritis	696.0
CREST syndrome or scleroderma	710.1
<b>Comorbidity</b>	
Diabetes	250
Chronic kidney disease	582, 585, 586
Cardiovascular disease (i.e., myocardial infarction, coronary artery bypass graft, unstable angina, angina pectoris, peripheral artery disease, heart failure, atrial fibrillation)	402.01, 402.11, 402.91, 410, 411, 413, 414.0 (exc. 414.02-07), 414.02-07, V45.81-82, 440.2, 433.9, 444.2, 427.3, 428
Cerebrovascular accident (i.e., stroke and transient ischemic attack)	430-436, V12.54
Hypertension	401-405, 997.91
Dyslipidaemia	272
Dementia/Alzheimer's disease	290, 294.1, 331.2
Parkinson's disease	332
Mood and anxiety disorders	300.0, 300.2, 296.0, 296.1, 296.04, 296.14, 296.4, 296.44, 296.5, 296.54, 296.6, 296.7, 296.8, 296.2, 296.3, 298.0, 300.4, 311
Chronic hepatic disease	456.0-456.2; 571-573
<b>Autoimmune disease</b>	
Multiple sclerosis	340
Rheumatoid arthritis	714.0, 714.1, 714.2, 714.30, 714.32, 714.33,
Inflammatory bowel disease	564.1
Ankylosing spondylitis	720

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<i>Idiopathic thrombocytopenic purpura</i>	287.31
<i>Myasthenia gravis</i>	358.0
<i>Sjogren's syndrome</i>	710.2
Osteoporosis	733
Malignancy	140–239
Chronic obstructive pulmonary disease	490, 491, 492, 494, 496

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Abbreviations: ICD9-CM, International Classification of Disease, Ninth Revision, Clinical Modification classification; EULAR/ACR, European League Against Rheumatism and American College of Rheumatology.

**Table S2.** Annual (2017–2022) standardised incidence rate (per 100,000 person-years) of SLE, stratified by sex, age, and geographical area.

Variable		2017	2018	2019	2020	2021	2022
<b>First definition</b>							
Overall		4.99 (4.79–5.18)	5.46 (5.25–5.66)	4.46 (4.27–4.65)	5.07 (4.87–5.27)	11.19 (10.89–11.48)	6.51 (6.29–6.74)
Sex	<i>Female</i>	9.08 (5.37–12.80)	8.91 (5.27–12.55)	7.61 (4.27–10.94)	7.54 (4.23–10.84)	18.33 (13.20–23.47)	8.87 (5.16–12.57)
	<i>Male</i>	0.91 (0–2.17)	2.23 (0.27–4.18)	1.31 (0–2.79)	2.61 (0.52–4.69)	3.91 (1.35–6.46)	4.27 (1.48–7.06)
Age	<i>18–29</i>	1.73 (0–5.11)	0	1.67 (0–4.93)	3.35 (0–7.99)	6.81 (0.15–13.49)	3.86 (0–9.22)
	<i>30–39</i>	1.77 (0–5.23)	3.56 (0–8.48)	5.39 (0–11.49)	1.83 (0–5.43)	7.52 (0.15–14.88)	2.13 (0–6.32)
	<i>40–49</i>	9.22 (2.83–15.61)	9.27 (2.85–15.69)	5.89 (0.73–11.06)	12.16 (4.63–19.70)	11.35 (3.94–18.77)	8.66 (1.73–15.60)
	<i>50–59</i>	8.78 (2.70–14.86)	5.29 (0.65–9.93)	3.09 (0–6.59)	7.12 (1.85–12.40)	18.15 (9.77–26.54)	6.54 (1.31–11.77)
	<i>60–69</i>	2.65 (0–6.32)	7.77 (1.55–13.99)	6.28 (0.78–11.78)	3.68 (0–7.85)	11.89 (4.52–19.27)	12.43 (4.73–20.13)
	<i>70–79</i>	3.21 (0–7.67)	4.63 (0–9.87)	7.48 (0.92–14.04)	1.46 (0–4.33)	14.22 (5.41–23.03)	4.45 (0–9.48)
	<i>80+</i>	7.02 (0–14.97)	8.94 (0.18–17.7)	2.09 (0–6.20)	3.92 (0–9.36)	5.67 (0–12.08)	5.85 (0–12.47)
Geographical area	<i>Northern Italy</i>	3.28 (3.05–3.52)	5.00 (4.72–5.29)	4.62 (4.35–4.90)	6.33 (6.01–6.66)	12.40 (11.95–12.86)	7.55 (7.19–7.90)
	<i>Central Italy</i>	7.92 (7.36–8.47)	7.69 (7.14–8.23)	4.86 (4.43–5.30)	3.63 (3.26–4.01)	10.76 (10.12–11.41)	5.03 (4.59–5.47)
	<i>Southern Italy &amp; Islands</i>	4.04 (3.74–4.35)	3.28 (3.00–3.55)	3.89 (3.59–4.19)	4.8 (4.47–5.13)	9.34 (8.88–9.80)	6.79 (6.40–7.19)
<b>Second definition</b>							
Overall		4.58 (4.40–4.77)	5.08 (4.88–5.27)	4.05 (3.87–4.22)	4.82 (4.63–5.02)	10.48 (10.19–10.76)	6.16 (5.94–6.38)
Sex	<i>Female</i>	8.69 (5.06–12.32)	8.52 (4.96–12.08)	6.85 (3.68–10.01)	7.54 (4.23–10.84)	16.84 (11.92–21.76)	8.06 (4.53–11.59)

Variable		2017	2018	2019	2020	2021	2022
	<i>Male</i>	0.46 (0–1.35)	1.78 (0.04–3.52)	1.31 (0–2.79)	2.17 (0.27–4.07)	3.91 (1.35–6.46)	4.27 (1.48–7.06)
Age	<i>18–29</i>	1.73 (0–5.11)	0	1.67 (0–4.93)	1.68 (0–4.96)	6.81 (0.14–13.49)	3.86 (0–9.22)
	<i>30–39</i>	1.77 (0–5.23)	3.56 (0–8.48)	3.59 (0–8.58)	1.83 (0–5.43)	7.52 (0.15–14.88)	2.13 (0–6.32)
	<i>40–49</i>	9.22 (2.83–15.61)	9.27 (2.85–15.69)	4.72 (0.09–9.34)	12.16 (4.63–19.7)	11.35 (3.94–18.77)	8.66 (1.73–15.6)
	<i>50–59</i>	8.78 (2.7–14.86)	5.29 (0.65–9.93)	3.09 (0–6.59)	7.12 (1.85–12.4)	16.13 (8.23–24.04)	6.54 (1.31–11.77)
	<i>60–69</i>	2.65 (0–6.32)	7.77 (1.55–13.99)	6.28 (0.78–11.78)	3.68 (0–7.85)	11.89 (4.52–19.27)	12.43 (4.73–20.13)
	<i>70–79</i>	1.61 (0–4.75)	3.09 (0–7.37)	7.48 (0.92–14.04)	1.46 (0–4.33)	14.22 (5.41–23.03)	4.45 (0–9.48)
	<i>80+</i>	4.68 (0–11.17)	6.71 (0–14.29)	2.09 (0–6.2)	3.92 (0–9.36)	1.89 (0–5.59)	1.95 (0–5.77)
Geographical area	<i>Northern Italy</i>	2.81 (2.6–3.03)	5.00 (4.72–5.29)	3.65 (3.4–3.89)	5.76 (5.45–6.07)	11.97 (11.52–12.41)	7.55 (7.19–7.9)
	<i>Central Italy</i>	7.33 (6.8–7.87)	7.12 (6.6–7.65)	4.86 (4.43–5.3)	3.63 (3.26–4.01)	9.1 (8.5–9.69)	4.47 (4.05–4.88)
	<i>Southern Italy &amp; Islands</i>	4.04 (3.74–4.35)	2.42 (2.18–2.66)	3.89 (3.59–4.19)	4.8 (4.47–5.13)	9.34 (8.88–9.8)	6.07 (5.7–6.45)
<b>Third definition</b>							
Overall		6.23 (6.02–6.45)	6.22 (6.01–6.44)	5.02 (4.82–5.22)	5.90 (5.69–6.12)	14.68 (14.34–15.02)	9.67 (9.40–9.95)
Sex	<i>Female</i>	10.66 (6.64–14.69)	10.46 (6.51–14.4)	8.75 (5.17–12.32)	9.05 (5.43–12.66)	22.82 (17.1–28.55)	13.3 (8.76–17.84)
	<i>Male</i>	1.82 (0.04–3.61)	2.23 (0.27–4.18)	1.31 (0–2.79)	2.61 (0.52–4.69)	6.08 (2.89–9.26)	6.17 (2.82–9.52)
Age	<i>18–29</i>	3.45 (0–8.24)	0	1.67 (0–4.93)	3.35 (0–7.99)	8.52 (1.05–15.98)	3.86 (0–9.22)
	<i>30–39</i>	1.77 (0–5.23)	3.56 (0–8.48)	5.39 (0–11.49)	5.5 (0–11.72)	9.4 (1.16–17.63)	6.4 (0–13.64)
	<i>40–49</i>	10.37 (3.6–17.15)	11.59 (4.41–18.77)	7.07 (1.41–12.73)	12.16 (4.63–19.7)	22.7 (12.21–33.19)	11.55 (3.55–19.56)

Variable		2017	2018	2019	2020	2021	2022
	<i>50–59</i>	10.98 (4.17–17.78)	7.41 (1.92–12.9)	3.09 (0–6.59)	9.16 (3.17–15.14)	20.17 (11.33–29.01)	10.90 (4.14–17.65)
	<i>60–69</i>	3.97 (0–8.47)	7.77 (1.55–13.99)	7.53 (1.51–13.56)	3.68 (0–7.85)	14.27 (6.2–22.35)	17.40 (8.29–26.52)
	<i>70–79</i>	4.82 (0–10.27)	4.63 (0–9.87)	8.98 (1.8–16.17)	1.46 (0–4.33)	17.06 (7.41–26.72)	7.42 (0.92–13.92)
	<i>80+</i>	7.02 (0–14.97)	8.94 (0.18–17.7)	2.09 (0–6.2)	3.92 (0–9.36)	5.67 (0–12.08)	7.80 (0.16–15.44)
Geographical area	<i>Northern Italy</i>	4.83 (4.54–5.11)	6.34 (6.02–6.67)	5.49 (5.19–5.80)	6.33 (6.01–6.66)	16.6 (16.07–17.12)	11.24 (10.81–11.68)
	<i>Central Italy</i>	9.11 (8.51–9.70)	8.29 (7.72–8.86)	5.42 (4.96–5.87)	4.92 (4.49–5.36)	14.65 (13.89–15.4)	6.98 (6.46–7.50)
	<i>Southern Italy &amp; Islands</i>	4.95 (4.61–5.29)	3.28 (3.00–3.55)	3.89 (3.59–4.19)	6.44 (6.05–6.82)	11.12 (10.61–11.62)	10.41 (9.92–10.90)

**Table S3.** Annual (2017–2022) standardised prevalence (per 100,000 people) of SLE stratified by sex, age, and geographical area.

Variable		2017	2018	2019	2020	2021	2022
<b>First definition</b>							
Overall		36.04 (35.51–36.57)	39.75 (39.2–40.3)	42.73 (42.15–43.3)	46.13 (45.53–46.73)	55.6 (54.95–56.26)	60.57 (59.89–61.25)
Sex	<i>Female</i>	60.03 (50.49–69.58)	65.84 (55.94–75.73)	70.74 (60.58–80.91)	75.38 (64.94–85.82)	90.54 (79.14–101.9)	97.14 (84.88–109.4)
	<i>Male</i>	10.93 (6.55–15.3)	12.46 (7.85–17.08)	13.11 (8.42–17.8)	14.33 (9.44–19.22)	16.93 (11.61–22.24)	18.98 (13.1–24.86)
Age	<i>18–29</i>	22.45 (10.25–34.65)	21.97 (10.03–33.91)	23.32 (11.11–35.54)	26.8 (13.67–39.94)	34.07 (19.14–49)	38.65 (21.71–55.59)
	<i>30–39</i>	47.70 (29.71–65.69)	51.56 (32.8–70.32)	55.72 (36.11–75.33)	58.67 (38.34–78.99)	67.65 (45.56–89.74)	68.28 (44.63–91.93)
	<i>40–49</i>	48.40 (33.77–63.04)	56.77 (40.88–72.66)	63.66 (46.68–80.63)	77.85 (58.78–96.92)	90.8 (69.84–111.7)	105.41 (81.24–129.6)
	<i>50–59</i>	48.29 (34.03–62.56)	51.85 (37.34–66.37)	51.54 (37.26–65.83)	54.94 (40.29–69.59)	69.58 (53.17–85.99)	70.82 (53.61–88.03)
	<i>60–69</i>	34.44 (21.2–47.67)	41.46 (27.1–55.83)	45.2 (30.44–59.96)	46.62 (31.8–61.44)	57.09 (40.95–73.24)	68.36 (50.3–86.42)
	<i>70–79</i>	25.70 (13.11–38.29)	24.7 (12.6–36.81)	29.94 (16.82–43.06)	29.24 (16.43–42.05)	38.39 (23.91–52.87)	38.56 (23.74–53.38)
	<i>80+</i>	18.73 (5.75–31.71)	22.35 (8.5–36.21)	23.03 (9.42–36.63)	17.65 (6.12–29.18)	17.01 (5.9–28.12)	19.5 (7.41–31.58)
Geographical area	<i>Northern Italy</i>	42.93 (42.09–43.78)	45.05 (44.19–45.92)	47.93 (47.03–48.82)	52.74 (51.8–53.67)	63.38 (62.35–64.4)	69.93 (68.85–71)
	<i>Central Italy</i>	36.28 (35.1–37.47)	42.95 (41.66–44.24)	46.49 (45.15–47.83)	48.93 (47.55–50.31)	58.99 (57.47–60.5)	62.75 (61.19–64.31)
	<i>Southern Italy &amp; Islands</i>	23.72 (22.98–24.46)	26.38 (25.6–27.16)	29.00 (28.19–29.82)	30.92 (30.08–31.76)	37.26 (36.33–38.18)	41.87 (40.89–42.85)
<b>Second definition</b>							
Overall		31.09 (30.6–31.58)	34.96 (34.44–35.48)	37.85 (37.31–38.39)	41.78 (41.21–42.35)	50.55 (49.93–51.18)	54.94 (54.29–55.59)
Sex	<i>Female</i>	54.50 (45.41–63.6)	60.42 (50.94–69.89)	64.66 (54.94–74.37)	70.1 (60.03–80.17)	83.81 (72.84–94.78)	89.48 (77.72–101.2)
	<i>Male</i>	6.37	8.01	9.18	10.85	13.45	15.19

Variable		2017	2018	2019	2020	2021	2022
		(3.03–9.71)	(4.31–11.71)	(5.25–13.10)	(6.6–15.11)	(8.72–18.19)	(9.92–20.45)
Age	18–29	22.45 (10.25–34.65)	21.97 (10.03–33.91)	23.32 (11.11–35.54)	25.13 (12.41–37.84)	32.37 (17.81–46.92)	36.72 (20.21–53.22)
	30–39	42.4 (25.44–59.36)	46.22 (28.46–63.99)	48.53 (30.23–66.83)	51.33 (32.32–70.34)	60.13 (39.3–80.96)	59.74 (37.62–81.86)
	40–49	47.25 (32.79–61.71)	55.61 (39.88–71.34)	61.3 (44.64–77.96)	75.42 (56.65–94.18)	88.28 (67.61–108.9)	102.52 (78.69–126.3)
	50–59	45.00 (31.23–58.77)	48.68 (34.62–62.74)	48.45 (34.6–62.3)	52.91 (38.53–67.28)	64.54 (48.73–80.35)	65.37 (48.84–81.91)
	60–69	29.14 (16.96–41.31)	36.28 (22.84–49.72)	40.18 (26.26–54.09)	41.71 (27.7–55.73)	52.34 (36.88–67.8)	63.39 (46–80.78)
	70–79	12.85 (3.95–21.76)	10.81 (2.8–18.81)	17.96 (7.8–28.13)	17.54 (7.62–27.47)	28.44 (15.98–40.9)	29.66 (16.66–42.66)
	80+	7.02 (0–14.97)	13.41 (2.68–24.14)	14.65 (3.8–25.51)	15.69 (4.82–26.56)	11.34 (2.27–20.41)	9.75 (1.2–18.29)
	Geographical area	Northern Italy	37.22 (36.43–38.00)	40.41 (39.59–41.23)	42.45 (41.61–43.29)	47.51 (46.62–48.4)	57.63 (56.65–58.61)
Central Italy		33.74 (32.6–34.88)	39.85 (38.61–41.09)	43.39 (42.1–44.69)	45.83 (44.5–47.17)	54.21 (52.77–55.66)	57.09 (55.6–58.58)
Southern Italy & Islands		16.75 (16.13–17.38)	18.91 (18.25–19.56)	22.65 (21.93–23.38)	26.27 (25.5–27.05)	32.79 (31.92–33.66)	36.64 (35.72–37.56)
<b>Third definition</b>							
Overall		42.44 (41.87–43.01)	46.43 (45.83–47.03)	49.90 (49.28–50.52)	53.74 (53.1–54.39)	66.55 (65.83–67.27)	74.20 (73.44–74.96)
Sex	Female	69.12 (58.88–79.36)	75.52 (64.92–86.12)	81.39 (70.49–92.29)	86.68 (75.49–97.88)	105.88 (93.55–118.2)	115.68 (102.31–129.0)
	Male	14.57 (9.52–19.61)	16.02 (10.79–21.25)	16.61 (11.33–21.89)	17.80 (12.35–23.25)	22.57 (16.43–28.7)	26.58 (19.62–33.53)
Age	18–29	27.63 (14.09–41.16)	27.04 (13.79–40.28)	28.32 (14.86–41.78)	31.83 (17.52–46.14)	40.88 (24.53–57.24)	46.38 (27.83–64.93)
	30–39	56.54 (36.95–76.12)	60.44 (40.13–80.76)	64.71 (43.58–85.84)	71.50 (49.07–93.93)	82.68 (58.26–107.1)	83.21 (57.11–109.32)
	40–49	56.47 (40.66–72.28)	66.04 (48.9–83.18)	74.27 (55.94–92.6)	87.58 (67.36–107.8)	112.24 (88.94–135.5)	131.4 (104.42–158.4)
	50–59	54.88	60.32	59.79	64.10	79.67	86.07

Variable		2017	2018	2019	2020	2021	2022
		(39.67–70.08)	(44.67–75.98)	(44.41–75.17)	(48.27–79.92)	(62.11–97.23)	(67.1–105.05)
	60–69	41.06 (26.61–55.51)	47.94 (32.5–63.39)	52.73 (36.79–68.67)	53.98 (38.04–69.93)	66.61 (49.17–84.05)	82.03 (62.25–101.82)
	70–79	32.13 (18.05–46.21)	30.88 (17.35–44.41)	37.42 (22.76–52.09)	36.55 (22.22–50.87)	48.35 (32.1–64.59)	48.94 (32.25–65.64)
	80+	21.07 (7.31–34.84)	22.35 (8.5–36.21)	23.03 (9.42–36.63)	17.65 (6.12–29.18)	17.01 (5.9–28.12)	21.45 (8.77–34.12)
Geographical area	Northern Italy	50.23 (49.32–51.15)	53.1 (52.16–54.04)	56.71 (55.74–57.69)	61.04 (60.03–62.05)	75.94 (74.82–77.06)	84.96 (83.78–86.15)
	Central Italy	42.42 (41.14–43.71)	49.07 (47.69–50.45)	53.18 (51.74–54.61)	56.32 (54.85–57.8)	69.65 (68–71.29)	75.11 (73.41–76.82)
	Southern Italy & Islands	28.76 (27.95–29.57)	31.29 (30.44–32.14)	33.82 (32.94–34.7)	37.40 (36.48–38.33)	45.55 (44.53–46.57)	54.41 (53.29–55.53)



**Figure S1.** Graphical algorithm depicting the three different SLE definitions.