Supplementary Materials and Methods

Disease-related symptoms and signs

By means of structured questionnaire, patients were asked if they had ever experienced or had been told by a physician that they manifested any of the following disease-related symptoms and signs: fever, weight reduction, anorexia, lymphadenopathy, tiredness, photosensitivity, malar rash / other skin rashes, alopecia, ulcers, arthritis/arthralgias, myalgias, tendonitis, neurologic disease/epilepsy, anxiety, visual disturbances, headaches, xerophthalmia/dry mouth, dyspepsia, chronic diarrhea, pericarditis, angina/chest pain, arrhythmia, arrhythmia/palpitations, dyspnea, extremities edema / vessel thrombosis, pleurisy, cough / signs and symptoms of respiratory infections.

Assessment of comorbidities

The following comorbidities were assessed by means of a structured questionnaire and were further ascertained by medical charts screening and use of relevant medications: allergies (allergic rhinitis, asthma, urticaria, drug allergies), diabetes mellitus, hypertension, hyperlipidaemia, thyroid disease (cancer, nodules, autoimmune thyroiditis), osteoporosis/osteoporotic fracture, heart disease, neurologic condition, cancer, kidney disease, lung disease, liver / gallbladder disease, peptic ulcer disease, blood disorders / thalassemia trait, skin diseases. The following mental conditions were also assessed: depression, generalized anxiety disorder, bipolar disorder, memory/cognitive disorder, eating disorders, alcohol dependence, illicit drug dependence, suicidal attempt. Viral infections were assessed by self-reporting and/or medical charts screening and no confirmatory essay was used. Patients were asked about any past or current medical history regarding tuberculosis, HIV, measles-mumps-rubella, infectious mononucleosis, cytomegalovirus, chicken pox.

Ultraviolet index in rural versus rural regions in Crete

Environmental measurements were provided by the National Observatory of Athens, which is recognized by the World Meteorological Organization (WMO) and collaborates with the Department of Chemistry at the University of Crete (http://ecpl.chemistry.uoc.gr/, http://finokalia.chemistry.uoc.gr/). The Ozone Monitoring Instrument (OMI) on board the NASA EOS Aura spacecraft is a nadir viewing spectrometer that measures solar reflected and backscattered radiation in a selected range of the ultraviolet and visible spectrum. Through a surface ultraviolet irradiance algorithm noontime surface spectral UV irradiance estimates of erythemal dose rate or the UV index (UVI) can be provided. UVI is an international standard measurement of the strength of sunburn-producing UV radiation at a particular place and time. The UVI is a dimensionless number and calculated by weighting the spectral UV irradiance from Sun and sky that is received on a horizontal surface, with the action spectrum for erythema, Integrating the weighted spectrum over the wavelength range 250–400 nm, and multiplying the result by a constant which is equal to 40 m2W−1 (WHO, 2002).

Supplementary Table S1. Structured form used to record active SLE manifestations according to the BILAG nomenclature [1]

Physician Global Assessment:

☐ mild SLE
☐ moderately severe SLE
☐ severe SLE

BILAG score [2]	Organs/domains	Year of appearance
Constitutional		
B	At least one from: a) fever >38°C, b) weight loss >10%, c) lymphadenopathy (peripheral or intra-abdominal/thoracic)	
Mucocutaneous		
B	At least one from: a) lupus rash and/or skin vasculitis involving 9–18% of BSA (with/without mild ulcers or gangrene), b) panniculitis involving <9% of BSA, c) angioedema without airway involvement, d) excessive hair loss / alopecia with inflammation of the scalp	
A	At last one from: a) lupus rash and/or skin vasculitis involving >18% of BSA and/or skin vasculitis with severe ulcers or gangrene), b) panniculitis involving >9% of BSA, c) angioedema with airway involvement	
Gastrointestinal		
B	At last one from: a) moderate ascites; b) moderate enteropathy and / or malabsorption syndrome; c) pancreatitis; d) lupus hepatitis with total-Bil <2.5 mg/dl and normal PT/PTT	
A	At least one from: a) severe ascites with acute abdomen; b) severe enteropathy and / or malabsorption syndrome; c) pancreatic insufficiency; d) lupus hepatitis with hepatic insufficiency; e) mesenteric vasculitis	
Respiratory		
B	At least one from: a) moderate pleural effusion (no hypoxemia); b) moderate interstitial lung disease (imaging) without gas exchange disturbance; c) pulmonary arterial hyperteion (PAH) with mPAP <55 mmHg; NYHA I-II stage; d) alveolitis/pneumonitis	
A	At least one from: a) severe pleural effusion with hypoxemia; b) extensive interstitial lung disease with gas exchange disturbance; c) PAH with mPAP >55 mmHg and NYHA III-IV stage; d) alveolar haemorrhage	
Musculoskeletal		
B	At least one from: a) mobility-limiting polyarthritis or involvement of large joints; b) myositis with a muscle strength reduction to ≥4/5	
A	Myositis with a muscle strength <4/5, and/or involvement of diaphragm, head-neck muscles, pharyngeal muscles	
Hematologic		
B	At least one from: a) leucopenia 1000-2500/µl; b) neutropenia 500-1000/µl; c) lymphopenia 500-1000/µl; d) thrombocytopenia 20-50 × 1000/µl; e) anemia with hemoglobin 8-10 g/dl	

A	At least one from: a) leucopenia <1000/µl, b) neutropenia <500/µl, c) lymphopenia <500/µl, d) thrombocytopenia <20 × 1000/µl, e) anemia with hemoglobin <8 g/dl, f) thrombotic thrombopenic purpura (TTP / TTP-like)	
Ophthalmologic		
B	At least one from: a) moderate keratitis; b) moderate anterior uveitis; c) moderate scleritis or episcleritis	
A	At least one from: a) posterior uveitis, b) optic neuritis, c) anterior ischemic optic neuropathy, d) severe keratitis, e) severe anterior uveitis, f) severe scleritis or episcleritis	
Cardiovascular		
B	At least one from: a) moderate or large pericardial effusion, b) myocarditis, c) non-infectious endocarditis. (Items A to C should be without hemodynamic instability or heart failure or valve dysfunction or arrhythmia)	
A	At least one from: a) large pericardial effusion; b) myocarditis; c) non-infectious endocarditis; d) aortitis or coronary artery vasculitis. (Items A to C are with hemodynamic instability or heart failure or valve dysfunction or arrhythmia)	
Neurologic		
B	At least one from: a) moderate psychiatric manifestation; b) aseptic meningitis; c) transient ischemic stroke; d) other neurologic event with mild / moderate deficit	
A	At least one from: a) CNS vasculitis, b) stroke, c) myelopathy, d) continued epileptic seizures or status epilepticus, e) neurological syndrome with moderate / severe neurological deficit, f) severe psychiatric manifestation	
Renal		
B	At least one from: (a) Nephritis class II; (b) Nephritis class V (a-b with proteinuria <3 g / 24 hr and normal renal function)	
A	At least one from: a) Class III / IV nephritis or mixed V + III / IV, b) nephritis of any class with: proteinuria ≥3 g / 24 hr and / or impaired renal function (serum creatinine elevation of ≥30%)	

	Use of immunosuppressive/biologic treatment (due to active SLE)	**Year**
	Ever use of: a) azathioprine; b) mycophenolic; c) belimumab	
	Ever use of: a) cyclophosphamide; b) rituximab	

[1] BILAG, British Isles Lupus Assessment Group; BSA, body surface area

[2] *Rheumatology*. 2005; 44: 902-6.

Supplementary Table S2. Prevalence of active SLE manifestations (BILAG system) according to the physician global assessment (PGA) of disease severity

		PGA of SLE severity		
Organs/domains	**BILAG score**	**Mild (48.5%)**	**Moderate (33.9%)**	**Severe (17.6%)**
Constitutional	B	0.0%	1.6%	1.1%
Mucocutaneous	B	0.0%	8.0%	0.8%
	A	0.0%	0.0%	0.3%
Gastrointestinal	B	0.0%	0.3%	0.3%
	A	0.0%	0.0%	0.0%
Respiratory	B	0.0%	3.5%	0.8%
	A	0.0%	0.0%	0.3%
Musculoskeletal	B	0.0%	3.7%	0.3%
	A	0.0%	0.0%	0.5%
Renal	B	0.0%	2.1%	1.3%
	A	0.0%	0.5%	5.6%
Neurologic	B	0.0%	3.7%	1.9%
	A	0.3%	0.5%	2.7%
Cardiovascular	B	0.0%	4.8%	1.1%
	A	0.0%	0.0%	0.3%
Ophthalmologic	B	0.0%	0.0%	0.0%
	A	0.0%	0.0%	0.3%
Hematologic	B	0.3%	5.3%	1.1%
	A	0.0%	0.0%	3.5%
Immunosuppressive or biologic treatments	Group 1 [a]	0.0%	21.1%	1.3%
	Group 2 [b]	0.0%	3.5%	14.7%
At least one organ-domain actively involved		0.5%	32.8%	17.6%

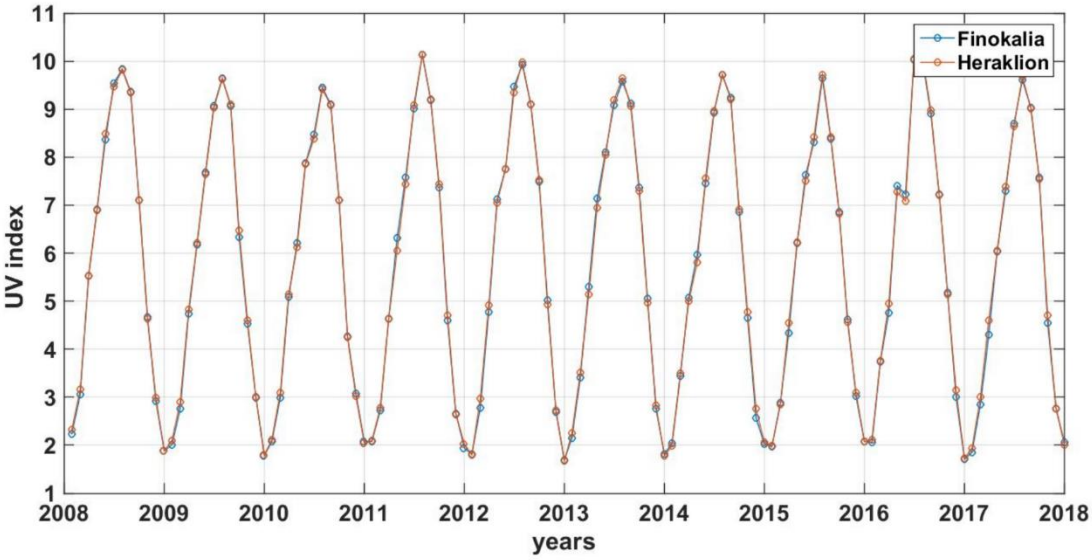
[a] Ever use of: a) azathioprine; b) mycophenolic; c) belimumab

[b] Ever use of: a) cyclophosphamide; b) rituximab

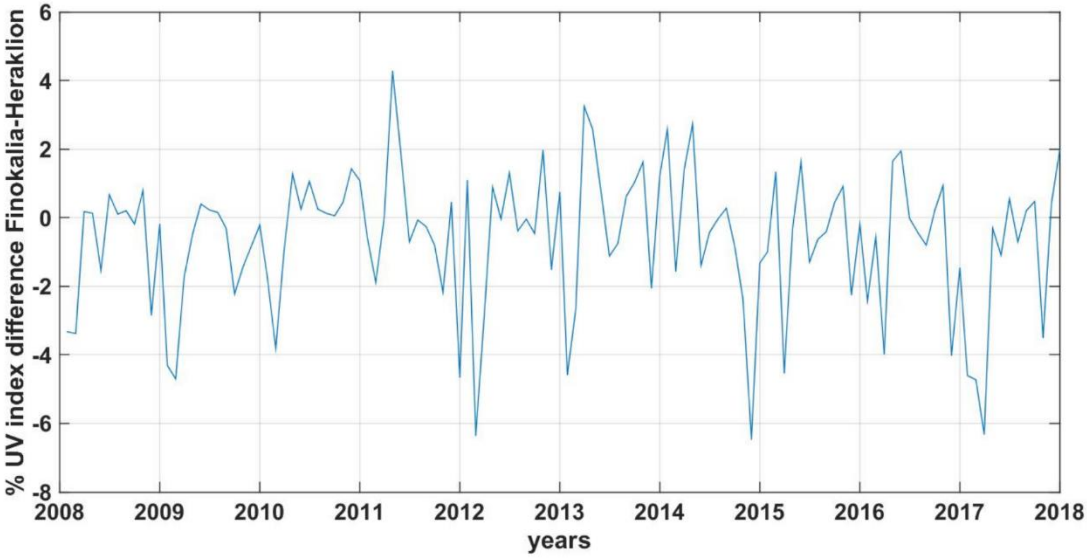
Supplementary Figure S1. UV index in rural (Finokalia village) versus urban (Heraklion city) areas of Crete over the time period 2008–2017

(A) Monthly mean, local noon UV Index for the rural area of Finokalia village (35.3N, 25.6E) and the urban area of Heraklion city (35.5N, 25.1E) in Crete by the OMI satellite sensor for the period 2008-2017. **(B)** Minimal (non-significant) differences (%) in the UV index between Finokalia and Heraklion areas over the time period 2008–2017.

A


Finokalia
Heraklion
UV index
years
11
10
9
8
7
6
5
4
3
2
1
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018

B


% UV index difference Finokalia-Heraklion
years
6
4
2
0
-2
-4
-6
-8
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018