Supplementary Appendix 1. Search strategy and data extraction

Search strategy

A keyword-based literature search was conducted in PubMed, Google and Google Scholar. Search terms are listed in **Supplementary Table 1** . Following identification of relevant citations, a bibliography search was conducted within the identified publications to detect additional pertinent citations. The full texts of all identified publications were screened and prioritized using the following selection criteria: filling a data gap (if they addressed a question for which limited or no data were available, regardless of scientific quality); nature and quality of the publication (good quality SLRs, followed by large, recent, well-conducted primary studies, followed by good quality narrative reviews); multiple biopsies (publications in which patients had ≥2 biopsies were prioritized); recent publications (there was no specific date cut-off, but papers published after 2010 were prioritized); countries (United States [US] and European data were prioritized). High-quality publications published prior to 2010, and non-US/European publications, were permitted. Although no formal study quality assessments were conducted, a combination of various parameters including recency of literature, sample size, and methodology detail were considered when prioritizing articles. There were no pre-defined exclusion criteria.

Literature search and data extraction

Overall, 248 citations were identified through the keyword-based search (n=117) and the bibliography search (n=131). which yielded 144 citations for prioritization. Of these, 26 were included in the pragmatic review (**Supplementary Figure 1**). Twelve publications were relevant to the first key research category (development of LN among patients with SLE; **Supplementary Table 2**). Twenty one publications provided information on the second research category (what happens within LN progression; **Supplementary Tables 3 & 4**). Finally, 22 publications answered the third key research category (progression to ESRD; **Supplementary Table 5**).

Supplementary Table 1. Publication search strategy

	Search terms
[publication terms] AND [lupus nephritis OR LN] AND [outcome terms]	('systematic review' OR 'review' OR 'meta-analysis' OR 'observational' OR 'cohort' OR 'registry' OR 'database' OR 'population based study') AND ('lupus nephritis' OR 'LN') AND ('progression' OR 'time to progression' OR 'Disease progression' OR 'proportion' OR 'percentage' OR '%' OR 'incidence' OR 'prevalence' OR 'clinical course' OR 'prognosis' OR 'severity stage')
[publication terms] AND [SLE terms] AND [renal terms] AND [outcome terms]	('systematic review' OR 'review' OR 'meta-analysis' OR 'observational' OR 'cohort' OR 'registry' OR 'database' OR 'population based study') AND ('systemic lupus erythematosus' OR 'SLE') AND ('Urinary abnormalities' OR 'Proteinuria' OR 'Haematuria' OR 'Haematuria' OR 'Albuminuria' OR 'Creatinine' OR 'Glomerular filtration rate' OR 'GFR' OR 'Glomerular disease' OR 'Renal involvement' OR 'Renal impairment' OR 'Early renal symptoms' OR 'renal failure' OR 'renal damage' OR 'nephritis' OR 'glomerulonephritis') AND ('progression' OR 'time to progression' OR 'Disease progression' OR 'proportion' OR 'percentage' OR '%' OR 'incidence' OR 'prevalence' OR 'clinical course' OR 'prognosis' OR 'severity stage')
[publication terms] AND [SLE terms] AND [ESRD terms] AND [outcome terms]	('systematic review' OR 'review' OR 'meta-analysis' OR 'observational' OR 'cohort' OR 'registry' OR 'database' OR 'population based study') AND ('systemic lupus erythematosus' OR 'SLE') AND ('end stage renal disease' OR 'ESRD' OR 'end stage kidney disease' OR 'ESKD') AND ('progression' OR 'time to progression' OR 'Disease progression' OR 'proportion' OR 'percentage' OR '%' OR 'incidence' OR 'prevalence' OR 'clinical course' OR 'prognosis' OR 'severity stage')

ESKD, end-stage kidney disease; ESRD, end-stage renal disease; GFR, glomerular filtration rate; LN, lupus nephritis; SLE, systemic lupus erythematosus

Supplementary Table 2. Proportion of SLE patients who develop LN

Author year (Publication type; country)	**LN definition**	**Follow-up (years)**	**Proportion of SLE patients that develop LN**
Adler 2006 (Primary study; UK)	• Biopsy consistent with the WHO classification (96%) or, in the rare event of them not having a biopsy (4%), if there were very strong supporting data implicating renal involvement attributable to SLE (diastolic blood pressure >90 mmHg requiring diuretic therapy; hypertension; proteinuria >0.5 g/24 h; creatinine clearance <60 ml/min; serum creatinine >124 µmol/l, in the absence of any other relevant disease)	8.9–15.1 (range of means for different ethnic groups)	• **During the course of disease:** LN developed in 127 of 401 (31.6%) SLE patients
Al Arfaj 2009 (Primary study; Saudi Arabia)	• Persistent proteinuria (proteinuria: >0.5 g/day, ≥3+ on urinary dipstick testing); persistently elevated creatinine, or presence of urinary sediments (cellular or granular casts) • Biopsy confirmation in ~90% patients	6.6 (mean)	• **During the course of disease:** LN developed in 299 of 624 (47.9%) SLE patients (female: 89.3%; male: 10.7%)
Croca 2011 (Primary study; UK)	• Biopsy-confirmed (~86.3%) • Unequivocal clinical, serological and urinary protein evidence of renal involvement (combinations of ≥2 of: diastolic blood pressure >90 mmHg requiring diuretic therapy; hypertension; proteinuria >0.5 g/24 h; creatinine clearance <60 ml/min; serum creatinine >124 µmol/l, in the absence of any other relevant disease)	5.0 (minimum follow-up period)	• **During the course of disease:** LN developed in 156 of 400 (39%) SLE patients (females: 91.6%; male: 8.4%) • Out of 400 SLE patients, RD developed among 81 (20.2%) after ≤1 year, 42 (10.5%) after 1 to ≤5 years, 23 (5.7%) after 5 to ≤10 years, and 10 patients (2.5%) after > 10 years of SLE diagnosis

			• Of all LN patients, 52% and 79% had been diagnosed within 1 and 5 years of onset of SLE, respectively
Galindo-Izquierdo 2016 (Primary study; Spain)	Biopsy-confirmed (in cases of LN relapse)	8.7 (median)	• **At SLE diagnosis:** Out of 3575 SLE patients, 245 (6.8%) had LN already at disease onset • **During the course of disease:** LN developed in 1092 of 3575 (30.5%) SLE patients (female: 85.7%; male: 14.3%) • Most patients with LN developed it in the first 12 months after SLE diagnosis: 56.3% and 82.6% in the first year and at 5 years, respectively
Hanly 2016; Hanly 2016a (Primary study; multinational)	• Renal disorder variable of the ACR classification criteria (persistent proteinuria and/or cellular casts) and/or biopsy evidence of nephritis as per ISN/RPS criteria (56.4% of the patients)	5.2 (mean)	• **During the course of disease**: LN developed in 700 of 1826 (38.3%) SLE patients (female: 85.6%; male: 14.4%) • Of these, 566 (81%) were identified at enrolment (mean 0.5 years after SLE diagnosis) and 134 (19%) were diagnosed during follow-up
Huong 1999 (Primary study; France)	• Abnormal renal biopsy by light microscopy examination, or 30% decrease in creatinine clearance over 1 year, or proteinuria > 1g/24 hr • Biopsy confirmation in 80% patients	7.7 (mean)	• **At SLE diagnosis**: 113 (26%) out of 436 SLE patients had renal involvement • **During the course of disease:** Renal involvement (nephritis) occurred in 180 of 436 (41.2%) SLE patients (female: 81.6%; male: 18.4%) • Sixty nine percent 69% of LN patients had developed it within 5 years of SLE onset

Mok 1999 (Primary study; China)	• Biopsy-confirmed	10. 8 (mean)	• **At SLE diagnosis**: 90 (22.1%), out of 406 SLE patients had RD • **During the course of disease**: LN developed in 183 of 406 (45%) SLE patients (female: 85.2%; male: 14.8%)
Narvaez 2017 (Primary study; Spain)	• Biopsy-confirmed	Not reported	• **During the course of disease:** LN developed in 190 of 429 (44.2%) SLE patients
Plantinga 2016 (Primary study; US)	• Documentation of urine abnormalities (documented at least twice; ≥500 mg protein in 24-hour urine, random urine protein ≥300 mg/dl, spot protein: creatinine ratio of ≥0.5, or positive urine cellular casts), or • Any renal biopsy consistent with LN classes II–VI, or • Documentation of LN by a treating rheumatologist or nephrologist in the medical record by 2005	7.8 (median)	• **During the first three years following SLE diagnosis,** LN developed in 119 of 344 (34.6%) SLE patients
Siso 2010 (Primary study; Spain)	• Biopsy-confirmed	17.4 (mean)	• **At SLE diagnosis:** 103 (15.3%) out of 670 SLE patients had LN • **During the course of disease:** Renal involvement occurred in 206 of 670 (31%) SLE patients (190 out of 206 LN patients were biopsy-proven LN cases) • Only 25 patients were diagnosed with LN >5 years after the diagnosis of SLE
Yokoyama 2011 (Review)	• NA	NA	• LN developed in 31%–65% of SLE patients in US and Europe, and in 45%–86% of SLE cases in Japan *(specific references not cited)*

			• Among Asian-Americans, the hazard ratio for LN relative to European Americans was 1.8 *(specific references not cited)*

ACR, American College of Rheumatology; LN, lupus nephritis; NA, not applicable; RD, renal disease; SLE, systemic lupus erythematosus; UK, United Kingdom; WHO, World Health Organization

Supplementary Table 3. Proportion of patients in different LN stages

Author year (Publication type; country)	Follow-up (years)	Sample size	Indication for renal biopsy	Classification criteria for LN	Proportion of patients in different LN stages
Adler 2006 (Primary study; UK)	8.9–15.1 (range of means for different ethnic groups)	122	Persistent proteinuria or haematuria for which no other cause could be found (e.g. urinary tract infection)	WHO	**At first renal biopsy:** • Class I: 1 (0.8%) • Class II: 7 (5.7%) • Class III: 17 (13.9%) • Class IV: 63 (51.6%) • Class V: 22 (18%) • Class VI: 1 (0.8%) • Not known (classified into other/mixed category): 11 (9%)
Al Arfaj 2009 (Primary study; Saudi Arabia)	6.6 (mean)	267	Clinical and laboratory signs of renal involvement	WHO	**At first renal biopsy:** • Class I: 3 (1.2%) • Class II: 54 (20.3%) • Class III: 30 (11.3%) • Class IV: 111 (41.6%) • Class V: 35 (13.1%) • Class VI: 8 (3%) Mixed Classes: 9.5% • Class II/III: 6 (2.2%) • Class II/V: 1 (0.3%) • Class III/IV: 5 (2%) • Class IV/V: 14 (5%)
Croca 2011 (Primary study; UK)	5.0 (minimum follow-up period)	139	NR	WHO	**1975–1985 (n = 17)** • Class I: 1 (5.8%)

					• Class II: 1 (5.8%) • Class III: 3 (17.6%) • Class IV: 11 (65%) • Class V: 1 (5.8%) • Class VI: 0 (0%) **1986–1995 (n = 36)** • Class I: 1 (2.7%) • Class II: 2 (5.6%) • Class III: 5 (14%) • Class IV: 18 (50%) • Class V: 9 (25%) • Class VI: 1 (2.7) **1996–2005 (n = 86)** • Class I: 0 (0%) • Class II: 3 (3.4%) • Class III: 15 (17.4%) • Class IV: 51 (59.5%) • Class V: 16 (18.6%) • Class VI: 1 (1.1%) **There were no significant differences between the three decades with respect to WHO class distribution**
Galindo-Izquierdo 2016 (Primary study; Spain)	8.7 (median)	1092	NR (Patients with histologically confirmed LN were recruited to study the profile of patients with renal involvement, in order to	WHO	**At first renal biopsy:** • Class I: 22 (2.5%) • Class II: 121 (13.6%) • Class III: 165 (18.6%) • Class IV: 433 (48.7%) • Class V: 92 (10.3%)

			improve guidelines on its systematic and standardized assessment)		• Class VI: 8 (0.9%) Mixed/Other classes: 5% • Class II+V: 10 (1.1%) • Class III+V: 9 (1.0%) • Class IV+V: 17 (1.9%) • Others: 12 (1.3%)
Hanly 2016, 2016a (Primary study; multinational)	Hanly 2016: 5.2 (mean); Hanly 2016a: 4.6 (mean)	377	The majority (86.6%) of renal biopsies were performed when nephritis was first suspected	ISN/RPS	**At first renal biopsy:** • Class I: 9 (2.39%) • Class II: 36 (9.55%) • Class III: 80 (21.22%) • Class IV: 129 (34.22%) • Class V: 65 (17.24%) • Class VI: 3 (0.8%) • Class III/V: 21 (5.7%) • Class IV/V: 34 (9.01%)
Howie 2003 (Primary study; UK)	6.6 (median)	182	NR	WHO	**At first renal biopsy:** • Class I: 11 (6%) • Class II: 28 (15%) • Class III: 29 (16%) • Class IV: 73 (40%) • Class V: 33 (18%) • Class VI: 8 (4%)
Huong 1999 (Primary study; France)	7.7 (mean)	175	Because of immunological features suggestive of high disease activity renal biopsy was performed in 25 patients (although	WHO	**At first renal biopsy (n=150):** • Class I: 3 (2%) • Class II: 29 (19.33%) • Class III: 32 (21.33%) • Class IV: 44 (29.33%)

			urinalysis / serum creatinine levels were normal), whilst 150 patients with abnormal urinalysis / elevated serum creatinine levels underwent >=1 biopsy		• Class V: 32 (21.33%) • Class VI: 2 (1.33%) • Others: 5.33% • Thrombotic microangiopathy: 4 (2.7%) • Interstitial nephritis: 3 (2%) • Focal segmental glomerulosclerosis 1 (0.7%) **At 2 and 3 biopsies (n=54)** • Class I: 3 (5.5%) • Class II: 4 (7.4%) • Class III: 8 (14.8%) • Class IV: 20 (37%) • Class V: 10 (18.5%) • Class VI: 7 (13%) • Others: 3.7% • Thrombotic microangiopathy: 1 (1.8%) • Interstitial nephritis: 0 (0%) • Focal segmental glomerulosclerosis: 1 (1.8%) **About 5% of renal biopsies showed a non-WHO glomerulonephritis pattern**
Kajawo 2017 (Primary study; South Africa)	NR	44	Active urine sediment, elevated Scr, urine abnormality (including active sediment, red cells present, proteinuria), elevated proteinuria	ISN/RPS	**At first renal biopsy:** • Class I: 2 (4.5%) • Class II: 10 (22.7%) • Class III: 7 (15.9%) • Class IV: 8 (18.1%) • Class V: 14 (32%) Mixed class: • Class V + IV: 3 (6.8%)

					At second biopsy: • Class II: 3 (7%) • Class III: 4 (9%) • Class IV: 19 (43.1%) • Class V: 5 (11.4%) • Class VI: 5 (11.4%) Mixed classes: 18.1% • Class V + III: 2 (4.5%) • Class V + IV: 6 (13.6%)
Mok 1999 (Primary study; China)	10. 8 (mean)	183	Proteinuria greater than 1 g/d of protein, microscopic haematuria (10 dysmorphic red blood cells/high-power field) or one or more red blood cell casts in urinary sediment, and abnormal renal function reflected by increasing serum creatinine level or declining GFR; indications for repeat renal biopsy were same as that of initial renal biopsy	WHO	**At first renal biopsy:** • Class I: 2 (1%) • Class II: 9 (5%) • Class III: 46 (25%) • Class IV: 101 (55%) • Class V: 25 (14%) **At repeat renal biopsy (26 static lesions + 11 progressive + 6 regressive lesions)** • Class III: 9 (27.91%) • **Class IV: 27 (62.79%)** • **Class V: 1 (9.3%)**
Momtaz 2017 (Primary study; Egypt)	3.7 (mean)	928	NR	WHO	**At first renal biopsy:** • Class II: 32 (3.5%) • Class III: 423 (45.6%) • Class IV: 398 (42.9%)

					• Class V: 75 (8%)
Moroni 2013 (Primary study; Italy)	21.9 (median)	89	NR	ISN/RPS	**At first renal biopsy:** • Class II: 1 (1.1%) • Class III: 11 (12.3%) • Class IV: 50 (56.1%) • Class V: 19 (21.3%) • Class III+V: 6 (6.7%) • Class IV+V: 1 (1.1%) • Not available: 1 (1.1%) **At repeat renal biopsy:** • Class II: 1 (3.7%) • Class III: 4 (14.8%) • Class IV: 11 (40.7%) • Class V: 6 (22.2%) Mixed classes: 18.5% • Class III+V: 3 (11.1%) • Class IV+V: 2 (7.4%)
Narvaez 2017 (Primary study; Spain)	NR	54	Renal biopsy was repeated only on the basis of one of following clinical indications: increase, persistence, or recurrence of proteinuria, nephrotic syndrome, or active urinary sediment (haematuria and/or cellular casts), or increase in serum creatinine level,	WHO or ISN/RPS	**At first renal biopsy:** • Class I: 0 (0%) • Class II: 9 (16%) • Class III: 9 (16%) • Class IV: 28 (52%) • Class V: 6 (11%) • Mixed (III/V+ V): 3 (5%) **At second biopsy**: • Class I: 1 (1.8%) • Class II: 2 (3.7%)

			or unexplained progression to renal failure.		• Class III: 8 (14.8%) • Class IV: 29 (53.7%) • Class V: 12 (22.2%) • Mixed (III/V+ V): 2 (3.7%)
Siso 2010 (Primary study; Spain)	17.4 (mean)	190	To assess the outcome of induction therapy (in 23 patients), and renal relapse (in 49 patients)	ISN/RPS	**At first renal biopsy:** • Class I: 8 (4.21%) • Class II: 33 (17.37%) • Class III: 40 (21.05%) • Class IV: 71 (37.37%) • Class V: 28 (14.74%) • Class VI: 3 (1.58%) Mixed classes: 4% • Type II+III LN: 5 (3%) • Type II+IV LN: 1 (0.5%) • Type III+V LN: 1 (0.5%) **The ISN/RPS type changed in 58% of repeat biopsies, most frequently from mesangial to proliferative (30%) and from focal proliferative to diffuse proliferative (22%)**
Tang 2015 (Primary study; China)	4.4 (mean)	681	NR (The aim of study was to assess clinicopathological characteristics and outcomes of biopsy proved lupus nephritis adult patients in China)	WHO or ISN/RPS	**At first renal biopsy:** • Class II: 40 (5.87%) • Class III: 76 (11.16%) • Class IV: 418 (61.38%) • Class V: 124 (18.21%) • Class VI: 23 (3.38%)
Yang 2015 (Primary study; China)	7.7 (mean)	1814	Re-biopsied for the worsening of RDs	ISN/RPS	**At first renal biopsy:** • Class II: 127 (7.0%)

			(including clinical symptoms, urine analysis and renal function); Repeat biopsies were performed in the majority of the patients with subsequent renal flares		• Class III: 244 (13.5%) • Class III+V: 202 (11.1%) • Class IV: 711 (39.2%) • Class V: 246 (13.6%) Mixed class: • Class IV+V: 284 (15.7%) **At repeat renal biopsy:** • Class II: 4 (12.1%) • Class III/III+V: 8 (24.3%) • Class IV/IV+V: 18 (54.5%) • Class V: 3 (9.1%)
Yokoyama 2004 (Primary study; Japan)	15.5 (mean)	60	NR (The study retrospectively analyzed 60 subjects with lupus glomerulonephritis who underwent renal biopsies and were followed for mean of 187 months)	ISN/RPS and WHO	**At first renal biopsy:** • Class I: 9 (15%) • Class II: 10 (16.7%) • Class III: 8 (13.3%) – Class III (A): 6 – Class III (A/C): 2 • Class IV: 23 (38.3%) – Class IV–G (A): 2 – Class IV–G (A/C): 15 – Class IV–S (A): 1 – Class IV–S (A/C): 5 • Class V: 10 (16.7%)
Yokoyama 2011 (narrative review; NA)	NA	NA	NA	NA	**The review provides the proportion by histological classes of LN for different countries from the cited studies** **At first renal biopsy:** **Japan (N=480)** • Class I: 15 (3.1%)

					• Class II: 77 (16%) • Class III: 62 (12.9%) • Class IV: 246 (51%) – Class IV–S: 51 – Class IV–G: 195 • Class V: 75 (16%) • Class VI: 5 (1%) **UK (N=507)** • Class I: 52 (10.3%) • Class II: 64 (12.6%) • Class III: 62 (12.2%) • Class IV: 233 (46.0%) • Class V: 96 (18.9%) • Class VI: 3 (0.6%) **USA (N=541)** • Class I: 5 (0.9%) • Class II: 54 (10.0%) • Class III: 107 (19.8%) • Class IV–S: 87 (16.1%) • Class IV–G: 111 (20.5%) • Class V: 159 (29.4%) • Class VI: 18 (3.3%) **China (N=327)** • Class IV–S: 20 (6.1%) • Class IV–G: 152 (46.5%) **France (N=71; white 63.3%, North African 17.4%, black 10.9%, Asian 8.7%)** • Class IV–S: 15 (21.1%)

					• Class IV–G: 31 (43.7%) **US (N=70; white 40.0%, black 30.3%, Hispanic 24.2%, Asian 9.1%)** • Class IV–S: 11 (15.7%) • Class IV–G: 22 (31.4%) **The ratio of Class IV–G in all Class IV was much higher in Asian countries (1:2.7–7.6) compared with the US and European countries (1:1.3–2.1)**

A/C, acute/chronic; Class IV–G, diffuse global (>50% of involved glomeruli have global lesions; Class IV-S, diffuse segmental (>50% of involved glomeruli have segmental lesions); GFR, glomerular filtration rate; HT, histological transformation; ISN/RPS, International Society of Nephrology/ Renal Pathology Society; LN, lupus nephritis; NA, not applicable; NR, not reported; RD, renal disease; Scr, serum creatinine; UK, United Kingdom; WHO, World Health Organization

Supplementary Table 4. Progression of LN across stages, time to progression and duration between two biopsies

Author year (Publication type; country)	**Criteria for LN classification**	**Overall sample size**	**Number of re-biopsied patients**	**Proportion of patients who have transformed between different LN stages**	**Time to progression within LN stages / duration between the two biopsies**
Collado 2016 (Primary study; Argentina)	ISN/RPS and WHO	41	18	• Histological transformation was observed in 17 of 18 re-biopsied patients – Class II -> Class III: 4 (23.5%) – Class II -> Class IV: 10 (59.0%) Class II -> Class V: 3 (17.5%)	• Median time to HT was 32 months (range, 11–305 months)
Huong 1999 (Primary study; France)	WHO	180	48	Histological transformation was observed in 24 of 48 cases, the most frequent being from focal to diffuse proliferative (23% of transformations) and from diffuse proliferative to chronic sclerosing glomerulonephritis (15%)	• Not reported
Kajawo 2017 (Primary study; South Africa)	ISN/RPS	44	44	• Most patients (65.4%) with a non-proliferative class of LN at first biopsy progressed into a proliferative class • Patients with initial proliferative LN at first biopsy (77.8%) remained as proliferative at repeat biopsy • At first and second biopsy, following histological transformations occurred – Class I -> IV: 2 (4.5%) – Class II -> II: 2 (4.5%), Class II -> III: 1 (2.2%), Class II -> IV: 3 (6.8%), Class II -> V: 1 (2.2%), Class II -> V+IV: 2 (4.5%) and Class II -> VI: 1 (2.2%) – Class III -> II: 1 (2.2%), Class III -> III: 2 (4.5%), Class III -> IV: 2 (4.5%), Class III -> V: 1 (2.2%) and Class III -> V+IV: 1 (2.2%)	• Biopsy interval was 2.8 years (mean)

				– Class IV -> III: 1 (2.2%), Class IV -> IV: 6 (13.8%) and Class IV -> VI: 1 (2.2%) – Class V -> IV: 4 (10%), Class V -> V: 2 (4.5%), Class V -> V+III: 2 (4.5%), Class V -> V+IV: 3 (6.8%) and Class V -> VI: 3 (6.8%) – Class V+IV -> IV: 2 (4.5%) and Class V+IV -> V: 1 (2.2%)	
Mercadal 2002 (Primary study; France)	WHO	66	29	About 14 patients had undergone transition from membranous LN with no or mild mesangial proliferation (Va and Vb), to a proliferative LN, 3 patients had progressed to fibrosis (which I think is Class VI), and 12 remaining the same	• The mean probability of transformation into a PLN from Class Va and Vb MLN at 1, 5, and 10 years was 3%, 8%, and 35%, respectively • Patient underwent a second renal biopsy after 10.9±1.1 years of follow-up
Mok 1999 (Primary study; Hong Kong)	WHO	183	43	• Twenty-six biopsy specimens showed static lesions (Class III to III, 9 cases; Class IV to IV, 16 cases; and Class V to V, 1 case) • 11 biopsy specimens showed progressive lesions - Class III to IV: 9 cases - Class II to IV: 1 case - Class V to IV, 1 case) • 6 biopsy specimens had regressive lesions (Class IV to III, 3 cases; Class IV to V, 3 cases). Patients with initial Class IV nephritis were very likely to have a relapse of Class IV nephritis (16 of 22 patients; 73%). Conversely, ~ half (9 of 18 patients; 50%) the patients with initial Class III nephritis relapsed into Class IV lesion.	• NR

Moroni 2013 (Primary study; Italy)	ISN/RPS	89	27	• Transformation from one to another class was observed in 55.5% of cases • Following histological transformations occurred – Class III -> III: 1 (3.7%) and Class III -> IV: 1 (3.7%) – Class IV -> II: 1 (3.7%), Class IV -> III: 3 (11.1%), Class IV -> IV: 9 (33.4%), Class IV -> V: 3 (11.1%), Class IV -> III+V: 2 (7.4%) and Class IV -> IV+V: 2 (7.4%) – Class V -> IV: 1 (3.7%), Class V -> V: 2 (7.4%) and Class V -> III+V: 1 (3.7%) – Class V+III -> V: 1 (3.7%)	• Interval between the first and second biopsy was 6.7 years (mean)
Narvaez 2017 (SLR and Primary study; Spain)	WHO or ISN/RPS	686 in review and 54 in primary study	686 in review and 54 in primary study	<u>Systematic literature review results</u> • The rate of pathological class transformation in these studies ranged from 40% to 76% of cases (mean 53%). • Most of Class II (78%) switched to higher grade of nephritis i.e. worse renal prognosis • Most patients (73%) in a proliferative class (III, IV or mixed III/IV+V) remained in a proliferative class on repeat biopsy • Class V, transition noted in 43% patients with most 40% into proliferative <u>Study results</u> • Of the 54 repeat biopsies, class switches occurred in 27 (50%) patients • Proliferative classes at first biopsy (III, IV, or a combination of III/IV+V) (n=39):	• Interval between the first and second biopsy was 2 years (mean)

				– Histological change occurred in 41% of cases (16/39) - only 18% of them changed to a non-proliferative class, usually to a Class V (only 1 case improved to a Class II) – The rest remained in the proliferative class on the repeat biopsy • Non-proliferative classes at first biopsy: – Class II (7/9; 78%) -> to a higher grade of nephritis (Class III or IV in 5 cases and Class V in the other 2), resulting in worse renal prognosis. Histological change occurred less frequently in patients with Class V (2/6; 33%), but all cases switched to a proliferative class	
Yokoyama 2004 (Primary study; Japan)	ISN/RPS and WHO	60	22	• Eight patients changed their histologic classes during follow-up periods. • Four patients showing clinical relapse or worsening of proteinuria (each one of Class I, II, III, and IV–G) were diagnosed as Class V at the episodic renal biopsies. • Two patients initially diagnosed as Class IV–S (A/C) changed to Class IV–G (A/C) or –G(C) by the follow-up biopsies after 3 to 36 months. One patient, changed from Class V (pure membranous) to Class V+IV–G (A/C)	• Not reported
Siso 2010 (Primary study; Spain)	ISN/RPS	206	78	• A second renal biopsy was carried out in 72 (38%) patients, a third biopsy in 18 (9%), and a fourth biopsy in 5 (2%). The ISN/RPS type changed in 58% of repeat biopsies, most frequently from mesangial to proliferative (30%) and from focal proliferative to diffuse proliferative (22%). Of the repeat biopsied indicated by renal flare, 25 (51%) showed histologic transformation to more aggressive forms; 22 (47%) showed the same histologic type with chronic lesions.	• Not reported

Vandepapeliere 2014 (Primary study; Belgium)	ISN/RPS	98	43	• Out of the 98 cases of LN followed from disease onset, 24, 23 and 51 were classified as Class III, IVS and IV–G, respectively • Repeat renal biopsy was performed in 43 patients (12 Class III, six Class IV–S and 25 Class IV–G) • Of 43 patients at follow-up, 32 patients had some residual proliferative disease (Class III, IV–S or IV–G), while seven displayed Class I, II or V. No signs of LN could be detected in the four remaining re-biopsies. • Of note, good pathological outcome was not less frequent in any of the three subsets. Interestingly, only two IV–S cases on the first biopsy were classified as IV–G at re-biopsy and, conversely, only one IV–G became IV–S.	• Repeat renal biopsy was performed in after a mean ± SD follow-up of 30±21 months, on a per-protocol basis rather than on clinical need

A/C, acute/chronic; Class IV–G, diffuse global (>50% of involved glomeruli have global lesions; Class IV–S, diffuse segmental (>50% of involved glomeruli have segmental lesions); HT, histological transformation; ISN/RPS, International Society of Nephrology/Renal Pathology Society; LN, lupus nephritis; MLN, membranous lupus nephropathy; NR, not reported; PLN, proliferative lupus nephritis; SD, standard deviation; SLR, systematic literature review; WHO, World Health Organization

Supplementary Table 5. Proportion of patients that develop ESRD and time to ESRD progression

Author year (Publication type; country)	Follow-up (years)	Sample size		Proportion of patients that develop ESRD and time to ESRD progression
		SLE	LN	
Tektonidou 2016 (SLR)	NA	NA	NA	**From LN to ESRD:** • About 22% of patients overall and 44% of patients with Class IV lupus nephritis developed ESRD within 15 years • Estimated risk of ESRD at 5, 10, and 15 years of LN in developed countries (by year of observation): – Risk of ESRD at 5 years from LN diagnosis was 16% in the 1970s, then plateaued to 11% by the 1990s – ESRD risks at 10 years and 15 years showed steeper declines in the 1970s and 1980s, but also plateaued in 1993–1997 at 17% and 22%, respectively – Notable increase in the 10- and 15-year risks in late 2000s, but these did not appear to persist after 2011 • Estimated risk of ESRD at 5, 10, and 15 years of LN in developing countries (by year of observation): – Risks at 5 and 10 years were relatively stable over time at 12% and 19%, respectively, while there was a slight decrease in the 15-year risk to 26% in the late 2000s – Risks at 5 years were only slightly higher in developing countries than in developed countries during the 2000s, but 15-year risks were 10 percentage points higher in developing countries • Renal histologic class–specific ESRD risks: – ESRD risks were highest among patients with Class IV lupus nephritis, with 5-year, 10-year, and 15-year risks of 19%, 33%, and 44%, respectively, in studies from developed countries from 2000 to 2006 – Five-year risks in patients with Class V LN were low and generally decreased over time – The 5-, 10-, and 15-year risks in patients with Class V LN in developed countries from 2000 to 2006 were 4%, 11%, and 20%, respectively

Adler 2006 (Primary study; UK)	8.9–15.1 (range of means for different ethnic groups)	401	127	**From LN to ESRD:** • Out of 127 LN patients, 21 (16.5%) progressed to ESRD • 3 Class III; 13 Class IV; 1 Class V; 1 Class VI; 2 patients with no biopsy; 1 patients with antiphospholipid features had ESRD **Time to ESRD from LN:** • Mean time from onset of renal involvement to ESRD was 69.6 months • 14 patients out of 21 progressed to ESRD within the first 5 years from LN diagnosis, while for seven it was >5 years
Al Arfaj 2009 (Primary study; Saudi Arabia)	6.6 (mean)	624	299	**From LN to ESRD:** • Out of 299 LN patients, 36 (12%) progressed to ESRD requiring dialysis
Croca 2011 (Primary study; UK)	5.0 (minimum follow-up)	~400	154	**From LN to ESRD:** • Of the 154 LN patients, 30 (19.5%) patients progressed to ESRD (29 were women) • Rate of ESRD evolution 5 years after RD: 6.9% during the first decade (1975–85), 7.7% during the second (1986–95) and 8.1% during the third (1996–2005); difference of ESRD rates was not statistically significant between decades • Patients of Afro-Caribbean origin have a higher ESRD rate within 5 years of RD (P = 0.001) **Time to ESRD from LN:** • On average, the time from RD to ESRD was 7.5 years; 43% during the first 5 years of RD, 37% between 5 and 10 years and 20% after 10 years • Overall, 5-year ESRD rate ranged from 7% to 8% • For patients who developed RD in the first 5 years, time from RD to ESRD was 1.9, 2.4, and 2.3 years in 1975–85, 1986–95, and 1996–2005 respectively
Galindo-Izquierdo 2016 (Primary study; Spain)	8.7 (median)	3575	1092	**From LN to ESRD:** • Out of 1092 LN patients, 113 (10.3%) developed ESRD

				• Amongst all ESRD patients, 45% received kidney transplant
Hanly 2016; Hanly 2016a (Primary study; Multinational)	5.2 (mean)	1826	700	**From LN to ESRD:** • Of the 700 LN patients, 87 (12.4%) progressed to ESRD • After 5 years, 62% of patients initially in estimated GFR state 3, and 11% of patients initially in estimated proteinuria state 3 transitioned to ESRD **From SLE to ESRD:** • The estimated cumulative incidence of ESRD (as defined by CKD stage 5 or by SDI) for the entire cohort at 5 years and 10 years following enrolment was 3.3 and 4.3% (reported in Hanly 2016a with mean follow-up 4.7 years)
Howie 2003 (Primary study; UK)	6.6 (median)	NR	182	**From LN to ESRD:** • Of the 182 LN patients, 40 (22%) patients went on to permanent dialysis
Huong 1999 (Primary study; France)	7.7 (mean)	436	180	**From LN to ESRD:** • Of the 180 LN patients, 14 (7.7%) developed ESRD despite therapy (12 of which had haemodialysis and 2 peritoneal dialysis)
Mercadal 2002 (Primary study; France)	6.9 (mean)	NR	66	**From LN to ESRD:** • Of the 66 LN patients, 8 (12%) progressed to ESRD • Four (28%) of the 14 patients with biopsy-proven proliferative LN progressed to ESRD indicating higher risk of ESRD in this subgroup
Mok 1999 (Primary study; China)	10. 8 (mean)	406	183	**From LN to ESRD:** • Of the 183 LN patients, 25 (13.6%) developed ESRD that required dialysis (4 haemodialysis and 21 peritoneal dialysis)

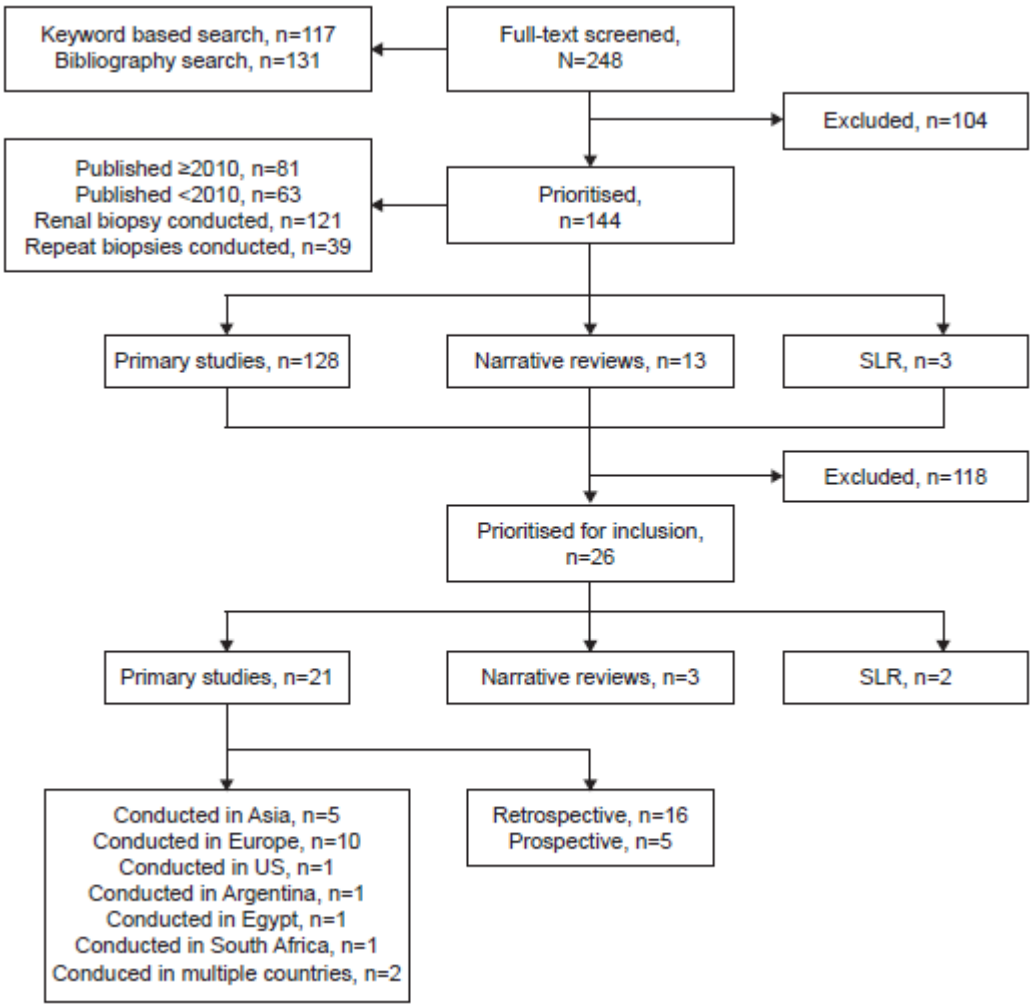
Momtaz 2017 (Primary study; Egypt)	3.7 (mean)	NR	928	**From LN to ESRD:** • The cumulative 5 years renal survival without dialysis was 90.3% (i.e. ESRD rate at 5 years was 9.7%)
Moroni 2013 (Primary study; Italy)	21.9 (median)	NR	89	**From LN to ESRD:** • Of the 89 LN patients, 12 (13.4%) progressed to ESRD
Narvaez 2017 (Primary study; Spain)	NR	NR	54	**From LN to ESRD:** • Of the 54 LN patients with at least 2 biopsies, 15 (28%) patients had unexplained progression to renal failure
Plantinga 2016 (Primary study; US)	7.8 (median)	344	119	**From LN to ESRD:** • Of the 119 patients with lupus nephritis, 23 (19.3%) developed ESRD **From SLE to ESRD:** • Of the 344 patients with SLE, 29 (8.4%) developed ESRD over 2,603.8 patient-years of follow-up • 5-year cumulative incidence of ESRD amongst SLE was 5.2% **Time from SLE to ESRD:** • The time to ESRD from SLE (defined by combined case definition) was approximately 4 years (median)
Siso 2010 (Primary study; Spain)	17.4 (mean)	670	190	**From LN to ESRD:** • Of the 190 LN patients, 18 (9.4%) progressed to ESRD
Tang 2015 (Primary study; China)	4.4 (mean)	NR	681	**From LN to ESRD:** • Of the 681 LN patients, 95 (14%) progressed to ESRD • Class IV patients had markedly higher rates of ESRD (17%) and Class V patients had low possibility of ESRD (2%)

Vandepapeliere 2014 (Primary study; Belgium)	6.4 (mean)	NR	98	**From LN to ESRD:** • Of the 98 LN patients, 4 (4%) progressed to ESRD and required renal replacement therapy (dialysis in two and transplantation in two) • 1 out of 23 Class IV–S LN (at a mean follow-up of 4.8 years) and 3 out of 51 Class IV–S LN (at a mean follow-up of 6.5 years) developed ESRD
Yang 2015 (Primary study; China)	7.7 (mean)	NR	1814	**From LN to ESRD:** • Of the 1814 LN patients, 201 (11.1%) progressed to ESRD • 11 (8.7%) Class II; 22 (9.0%) Class III; 16 (7.9%) Class III+V; 106 (14.9%) Class IV; 38 (13.4%) Class IV+V; 8 (3.3%) Class V LN patients developed ESRD
Yokoyama 2004 (Primary study; Japan)	15.5 (mean)	NR	60	**From LN to ESRD:** • Of the 60 LN patients, 10 (17%) reached ESRD (9 treated by haemodialysis and one treated by renal transplantation) • Patients with Class IV–S or IV–G at final biopsies showed higher rate of ESRD compared with that of Class I, II, III, or V (40.9% vs. 2.6%, P < 0.001)
Schwartzman-Morris 2012 (Narrative review)	NA	NA	NA	**From LN to ESRD:** • 5%–22% of SLE patients with RD progressed to ESRD requiring dialysis or transplant
Contreras 2002 (Narrative review)	NA	NA	NA	**From LN to ESRD:** • Of the 50 patients with Class V (A + B) LN, 5 (10%) reached ESRD after a mean follow-up of 5 years (Radhakrishnan 1993) • In Class IV, the probability of ESRD can be as high as 70% at 5 years (Austin and Balow 1999)

ACR, American College of Rheumatology; CKD, chronic kidney disease; Class IV–G, diffuse global (>50% of involved glomeruli have global lesions; Class IV–S, diffuse segmental (>50% of involved glomeruli have segmental lesions); ESRD, end-stage renal disease; GFR, glomerular filtration rate; LN, lupus nephritis; NA, not applicable; NR,

not reported; RD, renal disease; SDI, SLICC/ACR damage index; SLE, systemic lupus erythematosus; SLICC, Systemic Lupus International Collaborating Clinics; SLR, systematic literature review; UK, United Kingdom

Supplementary Figure 1. Literature screening metrics



SLR, systematic literature review; US, United States