Table S1: Search strategies

Database: PubMed	
#	**Search date: Sept 11, 2022**
1	("Hydroxychloroquine"[Mesh] OR Hydroxychloroquine[tiab] OR Sinonteam[tiab] OR Woodcock[tiab] OR Plaquenil[tiab] OR Quineprox[tiab])
2	("Pregnancy"[Mesh] OR pregnan*[tiab])
3	("lupus erythematosus, systemic"[Mesh] OR "antiphospholipid syndrome"[Mesh] OR "antibodies, antiphospholipid"[Mesh])
4	1 AND 2 AND 3
5	(animals[mh] NOT humans[mh])
6	4 NOT 5
7	(clinical trial[pt] OR comparative study[pt] OR multicenter study[pt] OR validation studies[pt] OR cohort studies[mh] OR cross-over studies[mh] OR case-control studies[mh] OR follow-up studies[mh] OR cross-sectional studies[mh] OR (case reports[pt] AND series[tiab]))
8	6 AND 7
9	(review[pt] OR review[ti] OR comment[pt] OR editorial[pt] OR meta-analysis[pt] OR meta-analysis[ti] OR letter[pt] OR in vitro techniques[mh] OR news[pt] OR guideline[pt])
10	8 NOT 9
11	10 AND eng[la]
Database: Embase	
#	**Search date: Sept 11, 2022** **Segment used: 1974 to Sept 11, 2022**
1	*Hydroxychloroquine/ or (Hydroxychloroquine or Sinonteam or Woodcock or Plaquenil or Quineprox).ti,ab.
2	exp pregnancy/ or (pregnan$).ti,ab.
3	1 and 2
4	exp systemic lupus erythematosus
5	exp antiphospholipid syndrome
6	exp antiphospholipid antibodies
7	4 or 5 or 6
8	3 and 7
9	limit 8 to english language
10	9 not ((exp animal/ or nonhuman/) not exp human/)
11	limit 10 to (yr="2012 -Current" and (conference abstract or conference proceeding or "conference review"))

12	limit 10 to (article or conference paper)
13	11 or 12
14	remove duplicates from 13
Database: Cochrane Central Register of Controlled Trials (CENTRAL)	
#	**Search date: Sept 11, 2022**
1	[mh "Hydroxychloroquine"] or Hydroxychloroquine or Sinonteam or Woodcock or Plaquenil or Quineprox:ti,ab,kw
2	[mh "Pregnancy"]or pregnan*:ti,ab,kw
3	[mh "systemic lupus erythematosus"] or [mh "antiphospholipid syndrome"] or [mh "antiphospholipid antibodies"]
4	#1 and #2 and #3
5	#4 not (pubmed or embase):an

Table S2: Standardized review protocol and study eligibility criteria based on the PICO framework

Category	**Inclusion criteria**
Population	• Pregnant women with systemic lupus erythematosus, antiphospholipid syndrome or positive antiphospholipid antibodies
Intervention	• Hydroxychloroquine
Comparison	• Any
Outcome	• High lupus activity (for SLE patients) • Preeclampsia • Intrauterine growth restriction
Study type	• Comparative studies (clinical trials and observational studies) • *Exclude:* Non-comparative studies
Language	• English
Publication date limits	• **Databases:** From inception to Sept 11, 2022 • **Conferences Proceedings:** Past 10 years from 2012 to 2022

Table S3: Assessment of bias risk using Cochrane Collaboration's Tool

Study	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Levy, R. A. 2001	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk

Table S4: Quality assessment of cohort/case-control studies using the Newcastle-Ottawa Scale

Study	Study design	Selection				Comparability	Outcome			Final score
		representativeness of the exposed cohort	selection of the non-exposed cohort	ascertainment of exposure	outcome of interest was not present at start of study	comparability of cohorts on the basis of the design or analysis	assessment of outcome	follow-up long enough for outcomes to occur	adequacy of follow up of cohorts	
Clowse, M. E. 2006	Cohort	*	*	*	*	*	*	*	*	8
Al Arfaj, A. S. 2010	Cohort	*	*	*	*	*	*	*	*	8
Leroux, M. 2015	Cohort	*	*	*	*	**	*	*	*	9
Sciascia, S. 2016	Cohort	*	*	*	*	*	*	*	*	8
Kroese, S. J. 2017	Cohort	*	*	*	*	**	*	*	*	9
Seo, M. R. 2019	Cohort	*	*	*	*	*	*	*	*	8
Abd Rahman, R. 2020	Cohort	*	*	*	*	**	*	*	*	9
Baalbaki, S. 2020	Cohort	*	*	*	*	**	*	*	*	9
Do, S. C. 2020	Cohort	*	*	*	*	*	*	*	*	8
Canti, V. 2021	Cohort	*	*	*	*	**	*	*	*	9
Gerde, M. 2021	Cohort	*	*	*	*	**	*	*	*	9
Liu, Y 2021	Cohort	*	*	*	*	*	*	*	*	8
Liu, J 2022	Cohort	*	*	*	*	*	*	*	*	8

Table S5: Study characteristics and availability

	Research type	Number of pregnancies	Study population	Treatment/Comparator Groups (n)	Outcomes reported
Levy, R. A. 2001	RCT, single center	20	SLE, DLE	a) HCQ (10) b) placebo (10)	lupus activity
Clowse, M. E. 2006	Prospective cohort, single center	257	SLE	a) No HCQ (163) b) HCQ (56) c) HCQ stopped (38)	lupus activity, IUGR
Al Arfaj, A. S. 2010	Retrospective study, single center	383	SLE	a) Prednisolone (222) b) Prednisolone + HCQ (69) c) Prednisolone + azathioprine (30) d) Prednisolone + azathioprine + HCQ (8) e) None (54)	IUGR
Leroux, M. 2015	Retrospective cohort, single center	118	SLE	a) HCQ (41) b) no HCQ (77)	lupus activity, IUGR, preeclampsia

Sciascia, S. 2016	Retrospective cohort, single center	170	aPLs	a) HCQ (51) b) no HCQ (119)	preeclampsia, IUGR
Kroese, S. J. 2017	Retrospective cohort, single center	110	SLE	a) HCQ (30) b) no HCQ (80)	lupus activity, preeclampsia
Seo, M. R. 2019	Retrospective cohort, single center	151	SLE	a) HCQ (80) b) no HCQ (71)	preeclampsia
Abd Rahman, R. 2020	Retrospective cohort, single center	82	SLE	a) HCQ (47) b) no HCQ (35)	IUGR, preeclampsia
Baalbaki, S. 2020	Retrospective cohort, single center	77	SLE	a) HCQ (47) b) no HCQ (30)	IUGR
Do, S. C. 2020	Retrospective cohort, single center	129	SLE	a) HCQ (53) b) no HCQ (76)	preeclampsia, IUGR
Canti, V. 2021	Prospective cohort, single center	74	SLE	a) HCQ (45) b) no HCQ (29)	preeclampsia, IUGR
Gerde, M. 2021	Retrospective cohort, single center	101	APS	a) HCQ + LDA + LMWH (69) b) LDA + LMWH (32)	IUGR, preeclampsia
Liu, Y 2021	Retrospective cohort, single center	88	SLE	a) HCQ (44) b) no HCQ (44)	preeclampsia
Liu, J 2022	Retrospective cohort, single center	96	APS	a) HCQ (59) b) no HCQ (37)	IUGR, preeclampsia

SLE: systemic lupus erythematosus; DLE: discoid lupus erythematosus; HCQ: Hydroxychloroquine; APS: antiphospholipid syndrome; aPLs: antiphospholipid antibodies; IUGR: intrauterine growth restriction

Table S6: High lupus activity during pregnancy

	HCQ (n/N)	**Comparison (n/N)**	**Criterion**
Levy, R. A. 2001	HCQ: 0/10	Placebo: 5/10	SLEDAI≥4
Clowse, M. E. 2006	HCQ: 29/56	no HCQ: 101/163 HCQ stopped: 32/38	SLEDAI increase ≥3
Leroux, M. 2015	HCQ: 7/41	no HCQ: 20/77	SLEDAI≥4
Kroese, S. J. 2017	HCQ: 2/30	no HCQ: 7/80	SLEDAI≥4
Overall	**HCQ: 38/137**	**no HCQ: 133/330**	

Table S7: IUGR

	HCQ (n/N)	**Comparison (n/N)**
SLE subgroup	**HCQ: 48/359**	**no HCQ: 116/656**
Clowse, M. E. 2006	HCQ: 11/49	no HCQ: 29/157 HCQ stopped: 7/34
Leroux, M. 2015	HCQ: 4/41	no HCQ: 22/77
Al Arfaj, A. S. 2010	HCQ: 13/77	no HCQ: 41/252
Abd Rahman, R. 2020	HCQ: 6/47	no HCQ: 10/35
Baalbaki, S. 2020	HCQ: 1/47	no HCQ: 3/30
Do, S. C. 2020	HCQ: 9/53	no HCQ: 3/76
Canti, V. 2021	HCQ: 4/45	no HCQ: 8/29

APS/aPLs subgroup	HCQ: 7/179	no HCQ: 4/188
Sciascia, S. 2016	HCQ: 0/51	no HCQ: 2/119
Gerde, M. 2021	HCQ: 3/69	no HCQ: 0/32
Liu, J 2022	HCQ: 4/59	no HCQ: 2/37
Overall	**HCQ: 55/538**	**no HCQ: 120/844**

Table S8: Result of sensitivity analysis for IUGR in SLE subgroup

Removed study	No. of pregnancies (HCQ vs Control)	RR (95% CI) [a]	I^2
Clowse, M. E. 2006	310 vs 499	0.72 [0.51, 1.03]	68%
Leroux, M. 2015	318 vs 579	0.93 [0.68, 1.29]	65%
Abd Rahman, R. 2020	312 vs 621	0.88 [0.64, 1.22]	68%
Al Arfaj, A. S. 2010	282 vs 404	0.74 [0.51, 1.06]	70%
Baalbaki, S. 2020	312 vs 626	0.84 [0.62, 1.15]	69%
Do, S. C. 2020	306 vs 580	0.70 [0.50, 0.96]	54%
Canti, V. 2021	314 vs 627	0.89 [0.64, 1.22]	66%

[a] RR was calculated using fixed-effect model in sensitivity analysis

Table S9: Preeclampsia

	HCQ (n/N)	Comparison (n/N)
SLE subgroup	**HCQ: 27/340**	**no HCQ: 64/412**
Leroux, M. 2015	HCQ: 3/41	no HCQ: 5/77
Kroese, S. J. 2017	HCQ: 2/30	no HCQ: 9/80
Seo, M. R. 2019	HCQ: 6/80	no HCQ: 14/71
Abd Rahman, R. 2020	HCQ: 2/47	no HCQ: 5/35
Do, S. C. 2020	HCQ: 7/53	no HCQ: 20/76
Canti, V. 2021	HCQ: 1/45	no HCQ: 4/29
Liu, Y 2021	HCQ: 6/44	no HCQ: 7/44
APS/aPLs subgroup	**HCQ: 10/179**	**no HCQ: 14/188**
Sciascia, S. 2016	HCQ: 1/51	no HCQ: 8/119
Gerde, M. 2021	HCQ: 1/69	no HCQ: 0/32
Liu, J 2022	HCQ: 8/59	no HCQ: 6/37
Overall	**HCQ: 37/519**	**no HCQ: 78/600**